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OBSERVATIONS IN THE USE OF CISTERNA MAGNA ESTIMATIONS IN NEUROSURGERY

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WITHIN recent years, a marked advance has been made in the diagnosis and accurate localization of gross surgical lesions of the brain and spinal cord. Many intracranial tumors, which formerly could at most be only suspected from the neurological signs elicited before the exploratory operation, are now being accurately localized by the ventricular aerograms as first described and developed by Dandy, and similarly, a large percentage of surgical lesions of a character to block the free flow of cerebrospinal fluid within the spinal arachnoid are now being differentiated with a greater degree of certainty by the combined pressure registration of lumbar and cisterna magna punctures, as first suggested by Ayer. The following observations have resulted from the utilization of both of these methods of diagnosis, with the further development of the cisterna magna estimation as a means not only of facilitating in selected cases the accurate localization of surgical lesions of the spinal cord but of the cerebral cortex itself.

The injection of air into the posterior horn of one or of both lateral ventricles by means of a blunt ventricular needle inserted through the cerebral cortex and then the use of röntgenograms to outline the ventricles in their various planes, make possible the accurate localization of many tumors dislocating, malforming or impinging upon and indenting the normal outline of the lateral and third ventricles; this information is of particular value in large frontal, temporosphenoidal and occipital tumors—the more silent areas of the cerebral hemispheres as compared with the parietal lobes, lesions of which are more easily disclosed by the usual neurological signs; ventricular aerograms in this clinic have seldom aided the diagnosis of anterior midbrain tumors and only occasionally of the subtentorial lesions when there is more or less complete obstruction of the ventricles. This method of diagnosis is thus limited to tumors that alter the normal ventricular shape and position and they are usually of the large subcortical type and therefore malignant. During the past twelve years in this clinic, 81 per cent. of all intracranial tumors in adults have been malignant, and if the dural (endotheliomata) and auditory nerve tumors (neuro-fibromata) are excluded, then the

true brain tumor of cortical or subcortical type (excluding the tuberculomata) is malignant in over 94 per cent. of the cases.*

Tumors of the spinal cord have been of less frequent malignancy—41 per cent. in this clinic; besides, there are other surgical spinal lesions of benign character which may obstruct the normal flow of cerebrospinal fluid in the spinal arachnoid theca, such as adhesions due to a former spinal meningitis or to a fracture-dislocation of the spinal column or to the kyphosis of a chronic tuberculous process, and each of these conditions, but especially that of tumor, may at times require all possible information regarding the lesion in order that the appropriate treatment be instituted at an early date; the negative value of the combined cistern-lumbar puncture estimations may also exclude a surgical lesion in favor of the vascular type of lesions, such as thrombosis, etc., and thus an exploratory laminectomy be avoided. Only too frequently in the past, an exploratory laminectomy has been performed with negative findings.

FIG. 1.—Case 962. J. B. Supracortical aerogram in a case of suspected meningeal tumor indenting the cortex of the left frontal lobe. The air was injected by the cisterna magna route with the patient lying upon the right side. The normal distribution of the air in the subarachnoid spaces of the sulci immediately excludes a supracortical lesion.

Beside the value of combined cistern-lumbar puncture estimations in suspected spinal lesions, the puncture of the cisterna magna with the slow injection of air to replace the withdrawn cerebrospinal fluid may be of great value in selected cases of suspected cerebral cortical lesions. In a case of suspected dural endothelioma over the left frontal area, 15 c.c. of air were injected slowly into the cisterna magna with the patient lying upon the right side; röntgenograms, with the patient still upon the right side, revealed the injected air in the subarachnoid spaces over the entire left cerebral hemisphere and in such a regular manner throughout the sulci that such a lesion compressing or obliterating the subarachnoid spaces could be excluded with a fair degree of certainty; thus, if a dural tumor or a supracortical lesion had been projecting into and indenting the cortex of this hemisphere, or if a chronic process had obliterated an area of the subarachnoid space, as may occur in cortical tumor and abscess formations, old localized meningitis or

* The term "malignant" is here used in the sense that the tumor recurs even after an apparent total extirpation; cerebral gliomata, therefore, are malignant, although they do not form metastases.

old subarachnoid hemorrhage with its fibrous tissue residue, adhesions, etc., then it would have been possible for this area to have been outlined by the röntgenograms since no air could have entered the subarachnoid spaces at the site of the lesion. To ascertain whether the changing of the body and head position of this patient from the right side to the left might cause the air to seek the higher level of the subarachnoid spaces over the right cerebral hemisphere, several röntgenograms were again taken later and it was interesting to note that the air was now found diffused evenly over the right cerebral cortex; in this manner, a possible cortical and supracortical lesion of the right hemisphere was excluded and it is possible that such a lesion could have been demonstrated by the method.

FIG. 2.—Case 1102. A. R. Ventricular aerogram in a case of combined internal and external hydrocephalus, due to a partial blockage of the excretion of the cerebrospinal fluid by unabsorbed basilar and supracortical hemorrhage occurring at the time of birth. The air was injected by the cisterna magna route with the patient in a sitting position and the moderately dilated lateral ventricles are clearly delineated.

To determine whether the lateral position of the patient at the time of the air injection into the cisterna magna was a factor in preventing the air from ascending into the fourth ventricle and thus into the lateral ventricles, a cisterna magna estimation was performed upon a patient having the condition of combined internal and external hydrocephalus in whom it was important to ascertain the amount of ventricular dilatation and therefore permanent damage, before considering the advisability of an operative method of cranial drainage; ordinarily, a ventricular estimation would have been made for this purpose, but in the hope that the cerebral puncture could be avoided, the less damaging route of the cisterna magna was attempted with the patient in the sitting posture and the head flexed acutely forward so that the chin rested upon the chest. After the injection of the air the patient maintained the upright position until the röntgenograms had been made. As indicated by the accompanying plate, it will be observed that the air did ascend into the fourth ventricle up into the third ventricle and into the lateral ventricles and

a marked dilatation of the lateral ventricles is beautifully depicted; in this manner, the necessary information of the ventricular dilatation was obtained and yet the added damage of a cerebral puncture through the cortex into the ventricle was avoided. This is indeed a marked advance and should always be attempted in selected cases first, rather than advising a ventricular puncture other than as a last resort. Ventricular estimations and röntgenograms as a diagnostic test have had a mortality of almost 10 per cent. in many clinics including this one and there is a distinct danger to life in its use in the presence of large surgically removable lesions; in those cases where no surgically removable lesion exists, naturally the danger to life of the test itself is slight, but there is a definite danger of permanent damage to these patients—not from the standpoint of motor or sensory impairments, but rather from that of emotional and personality changes, increased cortical irritability even to the degree of later convulsive seizures, persistent headaches, dizzy spells, etc.; to insert a blunt puncture needle through brain tissue in patients in the absence of a surgically removable lesion certainly does not improve their condition and such cerebral trauma cannot help but make the condition of the patient worse. Therefore it does seem that ventricular punctures should only be advised as a last resort for patients in whom a surgically removable lesion is most probable and when all other methods of diagnosis have failed to localize the lesion. Naturally in cases of cortical irritability and of epilepsy without an increased intracranial pressure and in possible meningeal processes, no ventricular punctures are to be considered.

Quincke, in 1890, first advocated lumbar puncture as the best clinical method of obtaining spinal fluid for examination; he considered cistern puncture a possible, but unsafe method for clinical use. Both methods had been used by investigators on laboratory animals, but in each instance it was necessary to expose the dura by incising the soft overlying fascial and muscular layers before puncture was attempted. Due to the bony anatomy in the lumbar region of these experimental animals, it was also necessary to perform a laminectomy, whereas the exposure of the dura in the suboccipital region did not necessitate laminectomy due to the absence of spinal processes. At this site, a large area of dura over the cisterna medullo-cerebellaris was exposed by simple flexion of the head after incision of the overlying skin, fascia and muscle. Cistern puncture, therefore, on the experimental animal was considered preferable to lumbar puncture.

In considering the clinical application of these laboratory methods, direct puncture of the cauda equinal theca in the lumbar region was the more rational procedure. The proximity of the vital medullary centres to the exploring needle in cistern puncture condemned this method for clinical use.

It was not until 1919 that Dr. J. P. Ayer, of Boston, with associates in the Army Neurological Service, first presented a paper advocating the use of cistern puncture in the treatment of meningococcic meningitis. In the course of the treatment of this condition by the injection of antimeningo-

coccic serum following lumbar puncture, it had been found, and in some cases even after repeated lumbar punctures, that it was impossible to withdraw a sufficient quantity of spinal fluid to be replaced by the serum; thus in a patient where 30 to 40 c.c. of fluid had previously been readily withdrawn, it was found that but a small quantity, 5 or 10 c.c. of fluid, could be obtained at later puncture. The clinical course of the illness, temperature, headache and cervical rigidity demanded continued serum therapy. The failure of lumbar puncture to drain sufficient spinal fluid was attributed to meningitic adhesions of the spinal theca above the lumbar region. A method of entering the cerebrospinal subarachnoid space at a higher level was therefore sought.

This stimulated further investigation, particularly in reference to the direct puncture of the cisterna medullo-cerebellaris. The direct puncture was first attempted on the cadaver and was followed by careful dissection to learn the relationship of the exploring needle to the neighboring anatomy, particularly the medullary centres. It was found that after extreme flexion of the head, that is with the chin resting on the chest, that the occipito-atlantoid ligament, which extends from the rim of the foramen magnum to a corresponding attachment on the axis or second cervical vertebra, was stretched to a degree exposing adequate space for the puncture of the underlying dura. The depth of the cistern in this location represented the distance from the dura to the posterior surface of the upper cervical cord and the medulla. It was found to be not less than 1½ cm. in the adult.

The technic of the direct puncture was developed with these observations in mind, and is as follows: The patient is placed on the left side with a thin pillow under the head so as to maintain a horizontal alignment of the cervical spine with the dorsal spine. With head flexed on the chest, and maintained so by the operator's left hand, the thumb of which is placed on the external occipital protuberance and gradually slipped downward toward the first cervical vertebra where a soft depression is felt, the site of the puncture is located. This represents the interspace between the foramen magnum and the first cervical vertebra. With the thumb marking this site, the needle is introduced into the soft part in the midline with the right hand on a plane of a line drawn between the external auditory meatus and the glabella. At a distance of from 4 to 5½ cm., a resistance caused by the occipito-atlantoid ligament is encountered. Slight pressure and sudden release of this resistance indicates that the needle has entered the cistern and removal of the stylet from the needle should permit the appearance of spinal fluid.

Doctor Ayer has reported over 2000 cistern punctures in which this technic has been used. In this series there were no deaths directly or indirectly attributable to cistern puncture, and he concluded that cistern puncture, by an experienced operator, is a safe procedure. One death has been reported by a German investigator in a series of 310 cistern punctures. A necropsy in this case revealed an abnormally placed cerebellar artery as the cause of death.

The contra-indications of cistern puncture are chiefly any conditions associated with a marked increase of the intracranial pressure to the degree of measurable papillœdema and "choked disc", or in conditions where one may suspect pathology that obliterates the cisterna, as by adhesions of tuberculous meningitis or of extreme internal hydrocephalus.

The indications for cistern puncture in their order of importance have been: (a) The treatment of meningococcic meningitis in the presence of spinal block due to adhesions; (b) the treatment of cerebrospinal syphilis and particularly of general paresis; (c) the early diagnosis of compression of the spinal cord; (d) to obtain spinal fluid when lumbar puncture has been unsuccessful or in the presence of spinal arthritic pathology; (e) for purposes of irrigation of the spinal canal in suppurative meningitis when combined with lumbar puncture.

FIG. 3.—No. 879. I. S. Ventricular aerograms obtained by the injection of air by the cisterna magna route in the case of a suspected subcortical tumor associated with a cortical irritability to the degree of producing convulsive seizures. The advisability of not increasing the existing cortical irritability by the ventricular punctures of the cortical route is self-evident and especially in the presence of a non-surgical lesion. The ventricles are normal in size, shape and position.

The cistern puncture was first used in this clinic as an aid to the early diagnosis of spinal block due to spinal cord tumors as advocated by Ayer in 1920, but it has also been employed to determine its value as a diagnostic method in other neurosurgical conditions. During the first three years, cistern punctures have been used for the injection of air into the basal cisterna by gradually replacing the cerebrospinal fluid; röntgenograms, after this procedure, demonstrated that the air assumed the following distribution: it usually was found in the supracortical subarachnoid spaces, particularly in the sulci; occasionally, however, the air passed directly into the ventricles and aerograms resembling those obtained by ventricular air injection were obtained.

Lipiodol, a heavy iodine and olive oil preparation, which shows a shadow with X-ray and was first advocated by Sicard and then by DeMartel, of Paris, as a substance which could be safely introduced into the spinal theca, was next injected by cistern puncture. This substance has been used in the localization of spinal block, as in cord tumors, by assuming a level at

the point of obstruction, which can then be shown by the X-ray. When injected by lumbar puncture, it is necessary to place the patient for an indefinite period, one hour or more, in the uncomfortable head-down position following the introduction of the lipiodol, whereas when injected by cistern puncture, it is only necessary that the patient sit in a comfortable position while the lipiodol sinks to the upper level of the spinal block. Cistern puncture was thus found preferable to lumbar puncture in this investigation. The injected lipiodol, however, was *not* a non-irritant in three cases at least, as Sicard and DeMartel both had affirmed and it has been necessary to discontinue the use of lipiodol in this clinic.†

FIG. 4.—Lateral view of same patient showing the right lateral ventricle of normal size, shape and position. The third ventricle is just visible.

The combined cistern-lumbar puncture has been employed in the demonstration of spinal arachnoid block and has been found of value. In this procedure, cistern and lumbar punctures are performed at the same time; pressure readings are taken at both levels and should, in the absence of obstruction, be the same. The withdrawal of fluid from the lumbar area should, in the absence of block, result in a corresponding fall in pressure at both lumbar and cistern levels; so also should the withdrawal of fluid from the cistern result in a proportionate lowering of the pressure at both levels. It has been observed that in complete blockage of the spinal theca, the spinal fluid distal to the lesion may only amount to 10 or 15 c.c., and that after this has been withdrawn further drainage is impossible. The Queckenstedt test in combined cistern and lumbar puncture becomes a valuable diagnostic method: upon compression of both jugular veins, there is normally a corresponding rise in pressure at both cistern and lumbar levels. In the presence of spinal block, a rise in pressure is apparent only at the cistern level and slightly, if any, at the lumbar area, depending upon the extent of the block. During the past three years in this clinic, thirty-six cistern punctures have been attempted upon both infants and adults, the age varying from sixteen months in the youngest patient to forty-five years in the oldest. There have been two unsuccessful attempts at cistern puncture:

† ANNALS OF SURGERY, January, 1926, pp. 32–41.

the first occurred in an infant with internal hydrocephalus (the type of case that should not be attempted), and as orientation was difficult, due to the distorted anatomy in the suboccipital region, only one attempt of puncture was made; at later operation of suboccipital exploration, however, it was found that the cisterna magna had been obliterated by the medulla and cerebellum—both having been forced down into the foramen magnum to the level of the second cervical vertebra. The second failure of cistern puncture occurred in a man of forty-five years of age, with a short thick neck; repeated punctures were unsuccessful and for fear of complications, a failure was recorded. At later operation, an extensive sarcoma of the upper cervical vertebræ was demonstrated.

Cistern puncture in this series has been found a safe procedure; the occasional difficulties of lumbar puncture are rarely observed. In this regard, some investigators have considered cistern puncture preferable to lumbar puncture.

In the serum treatment of cerebrospinal infections, particularly meningococcic meningitis and cerebrospinal syphilis, cistern puncture affords a ready approach to the cortical subarachnoid spaces and to the ventricles as demonstrated by the observation of air injected into the basal cisternal and subarachnoid system. Combined cistern-lumbar punctures are a valuable method for the early diagnosis of spinal arachnoid block, though no definite information is obtained as to the level of the blockage. The use of lipiodol injected into the spinal subarachnoid theca in order to facilitate the localization of the blockage is to be avoided for fear of its becoming an irritant, as it is non-absorbable and thus the seriousness of the condition of the patient is greatly increased; ordinarily, lesions in the spinal canal can be diagnosed early and accurately located by the usual neurological examinations and especially by carefully repeated sensory tests aided by the combined cistern-lumbar punctures, without the necessity of recourse to the injection into the spinal canal of substances such as lipiodol, which may produce complications by not becoming absorbed; it has not been possible in this clinic to remove all of it at later operation, as its numerous globules had become encysted at different levels of the spinal theca—chiefly in the caudal sac, but also above and below the level of the spinal lesion.

Impressions.—The experience of this surgical clinic in the use of cisterna magna estimations has been a satisfactory one in lesions of the spinal cord—using the combined cistern-lumbar puncture method to ascertain a partial or complete blockage of the spinal subarachnoid space and even of the spinal canal itself by observing any changes in the pressure and the oscillatory wave; the use of lipiodol has been most discouraging, but the injection of air has been most helpful, not only in lesions of the spinal cord, but particularly of the lesions affecting the cerebral cortex, such as meningeal and cortical tumors—supracortical hemorrhagic cysts and the organization-residue

of former localized meningitis and unabsorbed supracortical hemorrhage occurring at birth or at later cranial injury; the demonstration of combined internal and external hydrocephalus and then, of the greatest value, the demonstration of supracortical adhesions and cortical cysts at the site of a former cerebral injury in cases of Jacksonian epilepsy with and without operation at the time of the acute lesion and in those cases of attempted cranial drainage operations when the intracranial pressure was not lowered—the cause very often being due to blockage of the escape of the cerebrospinal fluid through the dural opening by a mass of supracortical adhesions.

There has been no mortality nor any damage whatsoever in the use of cisterna magna estimations in this series of thirty-six patients in this clinic.

NEUROGENIC SARCOMA

A CLINICAL AND PATHOLOGICAL STUDY

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The subcutaneous and intermuscular tissues of the arm, leg, popliteal space and chest wall are the favorite seats of a tumor process commonly designated as fibrosarcoma, spindle-cell sarcoma or fascial sarcoma. Based upon the belief that the great majority of these tumors are of neurogenic origin, Ewing has described them under the term of *neurogenic sarcoma*. Because of their comparative rarity the general surgeon does not encounter them with sufficient frequency to be familiar with their true nature. Their innocent appearance and accessibility to removal provide an inviting setting for a simple excision. The serious nature of these small movable subcutaneous tumors is generally not recognized, they are regarded as benign fibromas and are excised, usually under local anæsthesia. The result is a prompt local recurrence followed by repeated excisions and recurrences. The disease becomes progressively more extensive and soon reaches a stage when it is beyond either surgery or radiation and frequently results in death from pulmonary metastasis. The serious nature of cancer of the breast is now sufficiently recognized so that a narrow local excision is usually avoided and the disease is treated by radiation and radical surgery, whereas the small neurogenic tumor with many of the potentialities of a carcinoma of the breast is usually excised with a narrow margin and the recurrences treated in the same manner.

A review of the literature fails to reveal reports of any extensive series of cases observed over a sufficient period to permit deductions as to the best method of approach in the treatment of this disease. In 1922, Regaud,[2] J. Roux-Berger *et al.*, reported nine cases of fibrosarcoma treated in the Radium Institute of Paris. Three were treated by X-rays alone, four by radium alone, and two by a combination of the two agents. None of the patients were cured. They conclude that most of the tumors are radioresistant, regress slowly and are sterilized with difficulty. Those tumors which are most radiosensitive develop visceral metastasis. They state that from every point of view the operative tumors should be treated preferably by surgery, and believe that radiotherapy is indicated only in the inoperable tumors and as a post-operative measure. Küttner[3] advises wide excision of all tumors which are amenable to radical removal and reports 30 per cent. cured by this method. Seyerlin and Holzel[4] conclude that surgery followed by post-operative radiation is the method of choice in the treatment of these tumors.

There are several important features about this group of tumors which would lead one to expect a favorable prognosis in this disease. In the first place, although some of the more cellular tumors exhibit a high grade of malignancy, many of them grow slowly, and remain localized for a long time. Secondly, their superficial location, permitting early recognition and wide removal without the necessity of sacrificing vital structures, should render this one of the curable neoplastic diseases. In spite of these favorable factors, the final results have not been satisfactory. On the other hand, a small but definite group of cured cases encourages the belief that a detailed analysis of the entire series may reveal important factors which have contributed to the successes or failures, and permit deductions which may prove of value in pointing the direction in the future treatment of the disease. It is the purpose of this paper to present the problem from a clinical and pathological viewpoint, to discuss the clinical course, diagnosis and treatment of this disease based upon a study of seventy-five cases of neurogenic sarcoma treated in the Memorial Hospital in the last fifteen years.

Pathology.—Neurogenic sarcomas arise in all situations where connective tissue is found. The rate of growth varies with the structure. At first circumscribed, these tumors soon tend to infiltrate surrounding tissues and sometimes infiltrate and penetrate the walls of blood-vessels, producing metastases. Ewing and many others are of the opinion that the great majority of fibromas and fibrosarcomas of the skin and subcutaneous tissues are of neurogenic origin and designate them as neurofibromas and neurofibrosarcomas. Ewing gives the following classification of fibrous tumors of the nerve trunks:

1. Cutaneous neurofibroma. Fibroma molluscum, Recklinghausen's disease.

2. Neurofibroma of the subcutaneous and deeper nerve trunks. (*a*) Plexiform neurofibroma. (*b*) Visceral neurofibroma. (*c*) Neurofibrosarcoma (neurogenic sarcoma).

Neurofibrosarcoma.—In this group the subcutaneous and deeper nerve trunks give rise to tumors which are more cellular than the cutaneous fibromas. They occur at first as slowly growing, circumscribed, firm, movable masses lying in the subcutaneous tissues. The structure varies from benign neurofibroma to highly cellular malignant tumors with markedly atypical cell qualities and invasion of blood-vessels. With an increasing cellular composition and atypical qualities of the cells and a diminution in the matrix, the tumors are more active in their growth, and show a tendency to rapid recurrence and widespread metastasis. Between the two extremes are all transitions in malignancy depending upon the relative cellular and fibrous content of the tumors. Histologically, the cells frequently show an elongated and spindle form and are arranged in intertwining bundles. The very cellular growths appear as large polyhedral cells with little stroma. Giant cells may be a prominent feature, and myxomatous changes are frequently seen. Although typical structures are readily identified, the distinction between benign and malignant neurogenic tumors is at times difficult. Many fibrous compara-

tively cellular tumors are malignant and will recur after surgical removal. Ewing states that when the bulk of cells greatly exceeds the matrix the tumors are usually of active growth and recur.

Histological Classification.—Because of the marked variation in the structure of these tumors and the corresponding variation in the degree of malignancy, it seemed convenient to devise some plan of histological classification based upon their relative cellular and fibrous content. Whereas it is fully recognized that no sharp line of demarcation can be drawn, microscopic examination of a large number of these tumors reveals that they are divisible into several groups. A distinct relationship between histological structure and clinical course metastasis and final result has been demonstrated in this way.

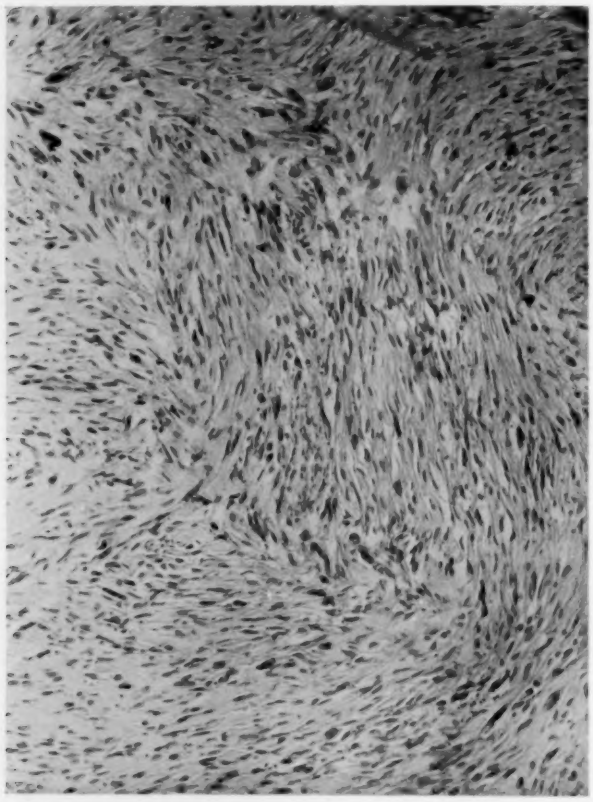

FIG. 1.—Photomicrograph showing neurogenic sarcoma of knee (Grade 1). This is the acellular fibrous type of growth which may be mistaken both histologically and clinically for simply fibroma. Each of three excisions was followed by prompt local recurrence. The patient is well seven years after amputation of the leg.

Myxosarcoma.—The structure of fascial myxosarcoma presents distinctive microscopic features which differ from those found in neurogenic sarcoma and permits a differentiation between these tumors histologically. The only cells recognizable in fascial myxosarcoma are those concerned in the formation of capillaries, cells which probably have their origin in the endothelium of capillaries. The stroma is composed of mucin. Their specific structure would favor the view that these tumors are not of neurogenic origin. Tumors of this type have been found to be radiosensitive.

A myxomatous structure is frequently seen in neurosarcoma and in some neurogenic tumors this element is so predominant that the neurogenic origin is difficult to determine. In many cases in which the primary tumor has shown a definite neurogenic structure the histological picture of later recurrences has shown marked myxomatous features. Changes of this type may be attributed to spontaneous degenerative processes and probably also to

effects produced by radiation. Clinical analysis of those cases in which a myxomatous structure has been prominent fails to show any distinctive clinical characteristics with the single exception that a large proportion have been located in the thigh. Typical fascial myxosarcoma has been encountered in only one case. Because of their specific structure it is believed that a special attempt to correlate the clinical course with the microscopic picture may yield data which will permit a clinical pathological grouping of these tumors. From our present knowledge, however, unless the structure is typically that of fascial myxosarcoma, those tumors in which a myxomatous element is present should be regarded as neurogenic. The true nature of the so-called fascial myxosarcomas and their relation to neurogenic sarcoma must be left open to further study.

The true neurogenic sarcomas may be divided into the following groups:

Grade 1.—Acellular, fibrous tumors composed of large spindle cells, lying in a dense stroma of hyaline fibrous material. Cells few in number, stroma abundant. (Low grade of malignancy.)

Grade 2.—Cellular tumors composed of large spindle cells arranged in compact intertwining bundles with whorl formation, very little intercellular substance, cells predominant. (Moderate grade of malignancy.)

Grade 3.—Very cellular tumors composed of small spindle cells arranged in whorls and fasciculi, or polyhedral cells growing diffusely in a loose fibrillar network. (Highly malignant.)

Age.—Of one hundred cases of neurogenic sarcoma the ages were as follows:

1–10 years	2 cases
10–20 years	6 cases
20–30 years	12 cases
30–40 years	24 cases
40–50 years	21 cases
50–60 years	22 cases
60–70 years	10 cases
70–80 years	3 cases

The youngest patient was six, the oldest seventy-two years of age.

Sex.—Of 100 cases, 60 were males and 40 females, giving a ratio of 6 to 4.

Trauma.—Fourteen patients out of a group of 72 gave a history of trauma which they associated with the appearance of the tumor. The determination of the rôle played by trauma in the genesis of tumors is most difficult. Whereas in most instances the association between the two is very remote and unlikely the relationship in some cases is suggestive. Chronic irritation or repeated traumatic insults are probably more important than a single injury. One patient whose occupation was a cutter developed a tumor on the thumb just at the point which was constantly irritated by scissors used in cutting cloth. One professional dancer developed a tumor of the inner aspect of the thigh which was subjected to repeated trauma in a dancing act. Although these cases are suggestive, they cannot be regarded as con-

clusively demonstrating this relationship. The absence of trauma and irritation in many cases with similar tumors in similar locations leaves the question open to further study.

The anatomical distribution of one hundred cases of neurogenic sarcoma was found to be as follows:

Lower extremity, 44: (Thigh, 29; popliteal space, 8; lower leg, 6; foot, 1.) Upper extremity, 20: (Upper arm, 11; forearm, 8; thumb, 1.)

Chest wall, 18; abdominal wall, 6; neck, 6; buttock, 2; axilla, 2; groin, 1; scalp, 1; total, 100 cases.

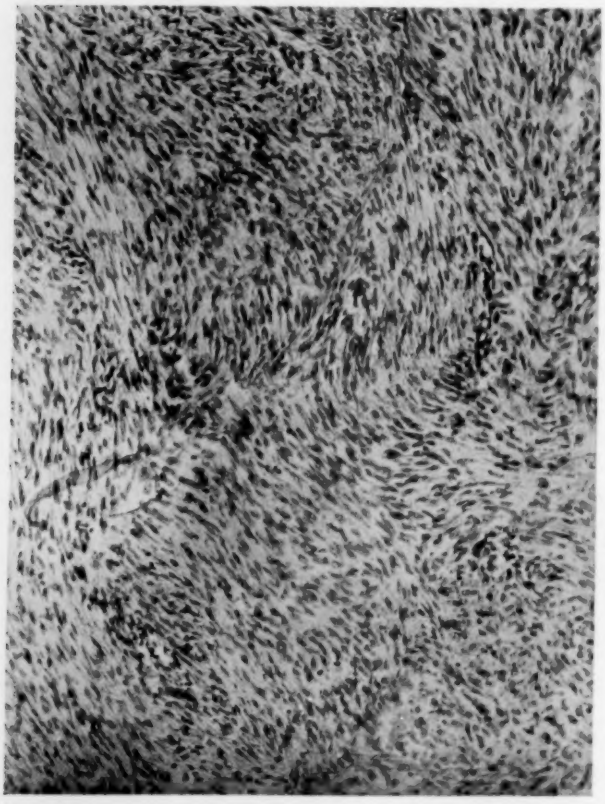

FIG. 2.—Photomicrograph showing neurogenic sarcoma (Grade 2). The structure is more cellular and less fibrous and presents the typical whorl formation characteristic of the neurogenic tumors.

Tumors of the Popliteal Space.—Of eleven neurogenic tumors of the popliteal space, two were primary and nine recurrent. The number of recurrences varied from one to seven. Five patients are alive and six are dead. An analysis of the cases which are well reveals that the treatment consisted of amputation in three instances, wide local excision in one and radiation alone in one. All three of the patients cured by amputation and free of disease, three, five, and seven years, respectively, had recurrent inoperable tumors. One large primary growth, 7 x 9 cm., was excised. The patient is free of disease two years and nine months. The tumor was well encapsulated and the line of excision wide of the disease. One large recurrent inoperable tumor measuring 7 x 9 cm., treated heavily with combined external and interstitial radiation (radium packs and bare tubes), is well and free of disease four and one-half years. The tumor gradually disappeared and was replaced by scar tissue; the functional result is excellent, with full motion in the knee.

Six patients with popliteal tumors failed to survive. One died of pulmonary metastasis twelve months after amputation. In this case two previous excisions were followed by rapid recurrences. A third local excision was performed, bare tubes were implanted in the operative wound and five weeks

later one radium pack was applied (18,000 mc. hrs. at 10 cm.). Two months later a local recurrence was observed, and amputation was performed, followed one year later by death from pulmonary metastasis. The structure of this tumor was extremely cellular and malignant and tumor cells were found growing in blood-vessels.

One advanced recurrent inoperable tumor of the popliteal region was treated with active deposit of radium and bare tubes. The patient died four months later of pulmonary metastasis. One very cellular recurrent tumor treated heavily with radium packs and bare tubes died of pulmonary metastasis two years after treatment was begun. One large recurrent tumor was treated with the radium pack (15,000 mc. hrs. at 10 cm.) and excised one month later. The tumor was encapsulated, measured 9 x 7 x 4 cm. and on section proved to be a highly cellular spindle and small cell vascular neurogenic sarcoma. No post-operative radiation was employed and the patient was free of recurrence for almost two years when he developed a local recurrence, and died soon afterward of pulmonary metastasis. One small recurrent tumor 2½ cm. in diameter disappeared under treatment with small doses of low voltage X-rays. The patient was apparently free of disease for four years when she developed pulmonary metastasis and died. One small primary tumor 2 x 3 cm. was excised and recurred four months later. The recurrence was treated with zinc chloride paste and radium packs. The patient died two months later of pulmonary metastasis.

It should be noted that the failures listed in the non-amputation group, treated by the more conservative methods of radiation or local excision or by both methods cannot be attributed to the advanced stage of the disease, as one presented a small primary growth 2 x 3 cm. in diameter and another a small recurrent tumor only 2 cm. in diameter. The two outstanding features in this group of cases are the inadequacy of the treatment employed and the highly malignant nature of the tumors. In one case no radiation was employed and the local excision of a small primary growth 2 x 3 cm. was followed six months later by death from pulmonary metastasis. In all the other cases radiation was of a miscellaneous variety and insufficient to sterilize a neoplastic process of the radioresistance known to be characteristic of these tumors.

Tumors of the Upper Extremity.—Out of five patients on whom an amputation was performed for neurogenic sarcoma of the upper extremity two are alive five and eight years respectively, and three died of pulmonary metastasis soon after amputation. Of the nine patients on whom no amputation was performed, three died and five are well five to nine years.

The Amputation Cures.—Of the two patients cured by amputation one had a tumor of the upper arm and one of the forearm. In one patient twenty-one excisions had been followed by as many recurrences. Two further attempts at local removal failed and amputation was finally performed. The patient is well five years after amputation. In the other case a recurrent tumor of the forearm failed to respond to buried radon implants and was

cured by amputation. The patient is well and free of disease eight years after amputation.

The Amputation Failures.—One patient with an extensive tumor of the upper arm was treated with bare tubes and later by amputation because of severe pain and œdema. Four months later a local recurrence was noted in the stump, and three months later death occurred from pulmonary metastasis. Histologically, the tumor was highly cellular and very malignant and a poor prognosis was predicted from the microscopic structure. In one recurrent tumor of the forearm, amputation was performed and followed eighteen months later by pulmonary metastasis, and death. No radiation was employed. Histologically, the tumor was cellular, very vascular and highly malignant. A small recurrent tumor of the wrist was subjected to amputation and followed four months later by recurrence in the stump and three years later by death from pulmonary metastasis.

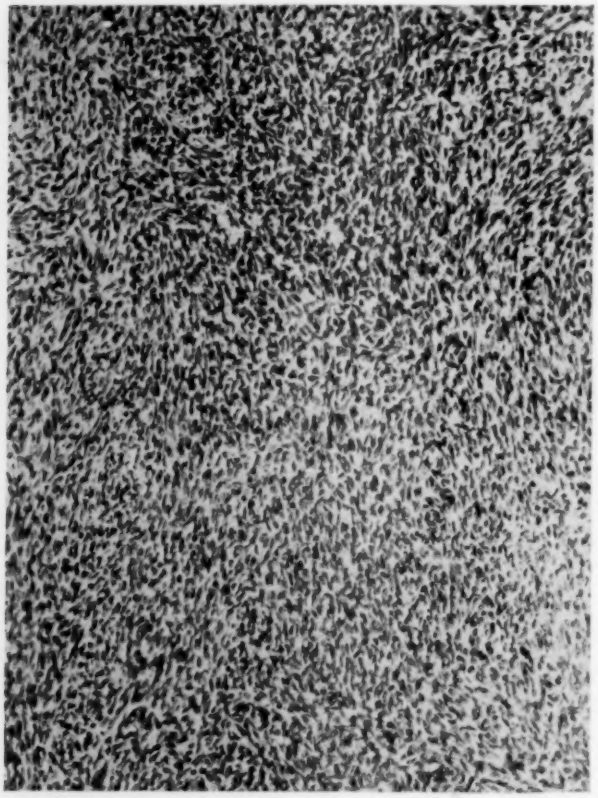

FIG. 3.—Photomicrograph showing highly cellular and malignant neurogenic sarcoma (Grade 3). The tumor is composed of small spindle and polyhedral cells closely packed with very little intercellular stroma. Neurogenic features are present but less distinct on account of the diffuse growth.

An analysis of this group with an attempt to determine any factors which may have contributed to the results reveals no relation between the extent of disease or number of previous recurrences and the final result. The one significant factor which seems to bear some relation to the results is the degree of malignancy of the tumor. In practically all the patients who died after amputation the structure of the tumor was unusually cellular. In the two instances tumor cells were found growing in blood-vessels. Contrasted with the highly cellular structure of the tumors in this group, the structure in the other group in which amputation was followed by cure was distinctly less cellular and more fibrous in character.

Cases Treated Without Amputation.—Nine patients with tumors of the arm were treated by the more conservative methods of radiation, local exci-

sion or both. Three of these died and six are living from two to nine years. The three patients who died had recurrent tumors which were treated by buried radon implants, alone in two instances and combined with local excision in a third. All developed repeated recurrences and finally died of pulmonary metastasis. The extent of disease in this group was not more advanced than in the group of six cases which are well. The method of treatment, however, differed markedly and it is to this that the difference in the results is attributed. Abstracts of the six patients free of disease from two to nine years appears in another section of this paper.

SUMMARY OF RESULTS OF TREATMENT OF TWENTY-FOUR NEUROGENIC TUMORS OF THE EXTREMITIES

Twelve well: Five amputation; seven non-amputation.

Non-amputation Group

(*a*) Prolonged external radiation of a large primary tumor of the arm followed by cautery removal. Well three years.

(*b*) Wide excision of a large primary tumor of the popliteal space. No radiation. Well three years.

(*c*) Extensive, recurrent, inoperable popliteal tumor treated by heavy external radiation and bare tubes. Well four and a half years.

(*d*) Small recurrent tumor of forearm excised and followed immediately by post-operative external radiation. Well seven years.

(*e*) Extensive, recurrent, inoperable tumor of upper arm treated by exposure and implantation of bare tubes, external radiation and Coley's toxins. Well six years.

(*f*) Recurrent tumor of arm excised and followed immediately by post-operative radiation with radium packs. Well nine years.

(*g*) Large recurrent tumor of arm excised, and the base treated with zinc chloride paste. Well five years.

Twelve died: Four amputation; eight non-amputation.

Non-amputation Group

(*a*) Five cases. Primary and recurrent tumors treated by repeated excision and inadequate radiation. Repeated recurrences followed by death from pulmonary metastasis.

(*b*) Extensive recurrent tumor treated with bare tubes and active deposit of radium. Death from pulmonary metastasis.

(*c*) Small primary growth in popliteal space excised. No radiation. Death from pulmonary metastasis four months later.

(*d*) Small recurrent tumor treated by inadequate external radiation. Death from pulmonary metastasis one year later.

Tumors of the Thigh.—Out of fifteen patients with tumors of the thigh, thirteen are dead and two are alive. The microscopic structure showed neurogenic sarcoma in five cases; myxosarcoma in five; and in five cases, the structure was essentially myxosarcoma but neurogenic features were present. Five patients had advanced primary growths; six had advanced recurrent tumors, two had early recurrent tumors, and one patient was admitted for post-operative radiation following the local excision of a recurrent tumor. Amputation was attempted in one case. A primary tumor 6 x 7 cm. on the anterior surface of the thigh was incised and a biopsy taken. The structure showed a myxosarcoma. Three months later an amputation was performed and followed eight weeks later by death from pulmonary metastasis.

The treatment of the other twelve patients who succumbed to the disease varied. In some cases it consisted of excision alone; in others, excision and implantation of bare tubes. The inoperable cases were treated mainly by exposure and insertion of bare tubes. Several patients were treated by zinc chloride paste alone or combined with radiation. In practically none of the cases was heavy external radiation employed. Many of these failures must be attributed to the advanced stage of the disease. That this is not the sole factor however is demonstrated by the following case:

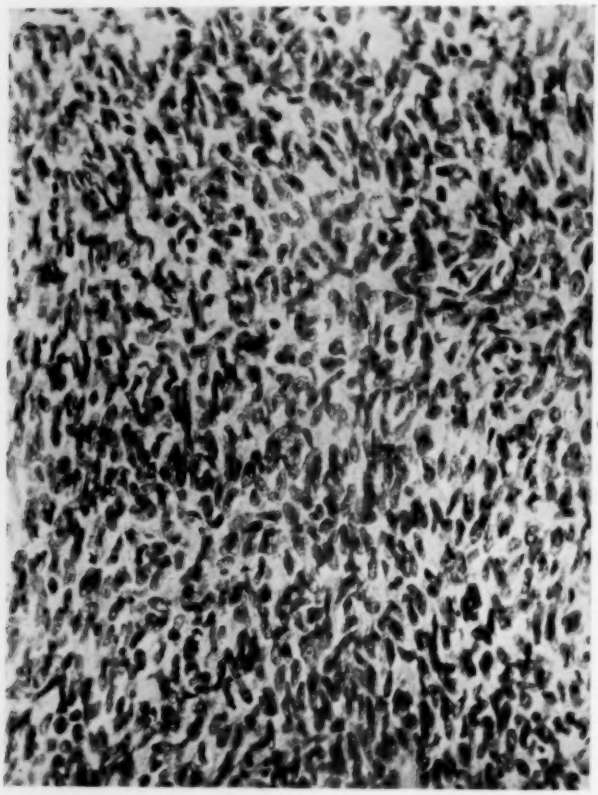

FIG. 4.—Photomicrograph showing high power of No. 3. Note the hyperchromatism and atypical quality of the cells and the numerous mitotic figures.

One small recurrent tumor 3 cm. in diameter, on the inner aspect of the thigh, was excised and bare tubes were implanted in the tumor bed. Examination of the specimen revealed a well-encapsulated tumor which microscopically proved to be a myxosarcoma probably of neurogenic origin. No external radiation was employed. Eight months later a local recurrence was observed which disappeared under external radiation but recurred. The patient died two years later of pulmonary metastasis. In this case the tumor was small and encapsulated—yet it recurred promptly and finally caused the death of the patient. It is believed that the failure to use post-operative external radiation may have been a factor in this result. Two of the fifteen patients with sarcomas of the thigh are well, two and five years, respectively, and are described in detail in a separate section of this paper.

Tumors of the Neck.—Out of five patients with neurogenic tumors of the neck, two died, two are good palliative results and one is free of disease, fifteen months after combined excision and radiation. Both patients who died had advanced recurrent tumors which were treated by small doses of external radiation. Two advanced inoperable tumors of the neck, one primary and the other recurrent, are being held in check by high voltage X-rays and

radium packs. Treatment was begun two years ago. The patients are in excellent general condition. The pain has been markedly relieved and the growth of the tumors arrested. One primary operable tumor was excised and the excision followed by one radium pack. The patient is free of disease sixteen months.

Tumors of the Chest Wall.—Out of nine patients with tumors on the chest wall five are alive and four died. Of those who died one had a very extensive tumor of the axilla which was treated by external radiation. The patient died two months after treatment was begun. One patient when first seen presented a mass on the shoulder 10 cm. in diameter, the fifth recurrence. Small doses of radiation and desiccation failed to control the disease and death occurred one year after treatment was begun. In the other two patients with recurrent tumors of the chest wall the disease was partly controlled by small doses of radiation, just insufficient however to completely eradicate the disease. They lived for five years and finally died of pulmonary metastasis.

Of the five patients who are well the growth of the tumor was arrested in three and two patients are free of disease. These patients have been under observation for only two and a half years, so the time is still too short to permit deduction as to ultimate results. One primary tumor of the shoulder treated by radium packs and low voltage X-rays has been held in check for two years. One extensive recurrent tumor of the shoulder has been held in check for one year by heavy external radiation. One primary tumor of the deltoid region treated with low voltage X-rays for one year failed to respond and was recently excised. One primary tumor of the shoulder excised and followed by post-operative radiation (low voltage X-rays) is free from recurrence one year. A recurrent tumor of the anterior chest wall heavily radiated and removed three months later by zinc chloride paste is free from recurrence one year.

Pulmonary metastasis.—Fifteen of the seventy-five patients (20 per cent.) are known to have developed pulmonary metastasis. Microscopic examination of the metastasizing tumors revealed a highly cellular structure in all. In four cases the structure was myxosarcoma. In the remainder of the group the tumors were very cellular and composed of small round and spindle cells actively growing and frequently invading the walls of the blood-vessels. In no case was pulmonary metastasis observed from the acellular fibrous type of growth. The relationship between the highly cellular nature of some of the tumors and their metastasizing property is very definite, so that the microscopic structure may serve as a fairly accurate and often useful guide in prognosis and treatment.

Radiation as an Aid to Diagnosis.—Although the clinical diagnosis of neurogenic sarcoma is relatively simple, occasionally these tumors may be confused with other lesions. Two instances in which an error in diagnosis was made illustrate the value of radiation as a diagnostic test. In one case an extensive primary soft part tumor of the back showed a phenomenal

response to radiation and disappeared almost entirely under treatment with radium packs. In another case a similar primary rapid regression and disappearance of a tumor of the buttock occurred. Both tumors presented all the clinical features of a neurogenic sarcoma. Later histological examination of the tumors revealed a very cellular malignant round and polyhedral cell tumor of undetermined origin in the first case and a lympho-sarcoma in the second. Neither tumor belonged to the class of neurogenic sarcomas.

In no case of neurogenic sarcoma, even of the most cellular variety, has a very rapid response to small doses of radiation been observed. This group of tumors in general is resistant to radiation and response occurs slowly and months after radiation of an intensive type. Small doses of radiation effect their growth to a very limited extent. In view of these observations a small dose of radiation, such as a single suberythema dose of low voltage X-rays, may serve as a useful diagnostic test in differentiating the radioresistant neurogenic sarcomas, from the radiosensitive tumors with which they may be confused, such as lymphosarcoma, or obscure malignant cellular tumors not of neurogenic origin. The test is of practical value from a therapeutic standpoint as the method of treatment is entirely different in the two instances. By detecting and excluding the highly malignant radiosensitive tumors not of neurogenic origin, surgery is scrupulously avoided, and these cases are treated by external radiation alone, whereas the attack upon the radioresistant neurogenic sarcoma is by the combined methods of surgery and radiation. Because of the fact that of the two varieties of tumors which simulate each other, one is extremely radioresistant and the other radiosensitive, the therapeutic test may be of considerable value in the differential diagnosis and may serve as a useful guide in treatment. The information obtained by this method may be sufficient to enable the execution of proper therapeutic

FIG. 5.—Photomicrograph showing cellular neurogenic sarcoma growing in blood-vessels. The patient died of pulmonary metastasis twelve months after amputation of leg.

measures without the necessity of incising the growth for biopsy. Whereas the latter procedure may be of little harm in case the growth proves to be a neurogenic sarcoma, the incision of a lymphosarcoma is distinctly harmful and is to be avoided.

Amputation.—Tumors of the extremity in which amputation offers a chance of completely eradicating the disease present an important problem in treatment. The decision between amputation on the one hand and excision and radiation on the other is at times most difficult. Out of ten amputations performed for neurogenic tumors of the extremity, five patients are well and five died of pulmonary metastasis soon after amputation. On the other hand, out of fifteen tumors of the extremity treated by local excision and radiation eight patients died and seven are alive from two to nine years.

In a comparison of the results of the two methods of treatment, a consideration of the extent of the disease in each group is most important. An analysis of the amputation failures reveals that the disease in these cases was not more advanced than in the group of successful amputations. In two patients the tumors were small primary lesions and in two others the recurrences were small, whereas several tumors cured by the more conservative methods of excision and radiation were advanced recurrent growths. The only tangible feature derived from a study of the amputation failures is the highly cellular and malignant nature of the tumors in this group. It would seem from our data that the success or failure to cure by amputation depends mainly upon the degree of malignancy of the tumor, the highly cellular growths being not infrequently followed by pulmonary metastasis.

Analysis of the results of treatment by the more conservative measures of excision and radiation reveal that seven out of fifteen patients are well from two to nine years. These results compare most favorably with those from amputation, especially since the extent of the disease was fully as great in this group as in the amputation group. Furthermore, an analysis of the eight failures indicates an outstanding inadequacy of the radiation employed compared with that employed in the cured cases.

Our results in the treatment of tumors of the extremities with reference to amputation seem to justify the belief that pre-operative radiation and wide local excision followed by prompt and adequate post-operative radiation is the method of choice in the treatment of the operable tumors. The procedure in the primary or recurrent inoperable tumors must be determined in each individual case and involves a consideration of a number of factors such as the extent of the disease, the expected functional result and the histological structure of the tumor. A number of excellent results by combined external and interstitial radiation encourage this procedure in advanced inoperable cases in which the growth is acellular and in which distant metastasis is unlikely. The decision between amputation and radiation in this group is very difficult and must remain open, awaiting further observations on the results of improved radiation therapy. It is believed that the radiation results can be vastly improved by increasing the doses of external radiation

to the limit of skin tolerance and combining with it interstitial radiation in selected cases.

DISCUSSION OF CURED CASES

In an analysis of the favorable results it is important to determine to what extent the cures are due to the early stage of the disease and the extent to which other factors such as the degree of malignancy and especially the type of treatment employed are responsible for the cures. In the five amputation cures the results are attributed primarily to the radical procedure of amputation. The nature and extent of the disease in this group is partly indicated by the number of previous recurrences which varied from three to twenty-three.

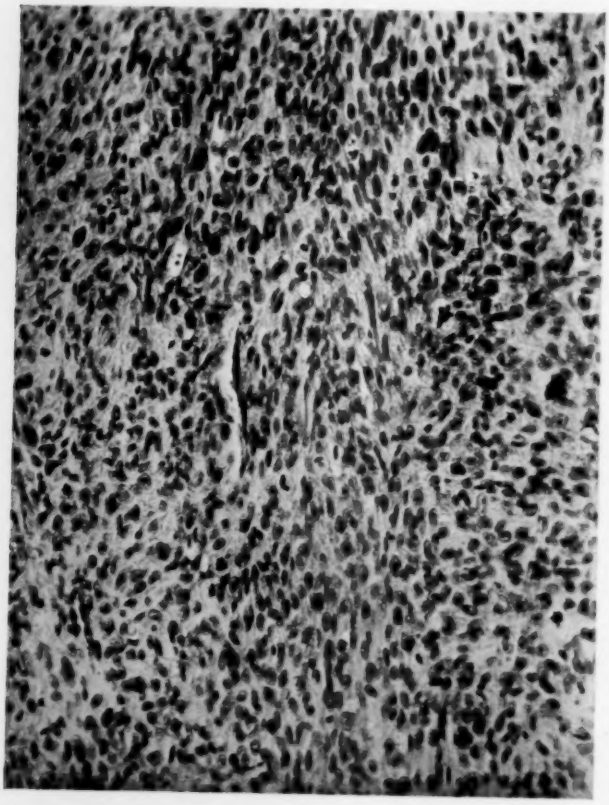

FIG. 6.—High power photomicrograph showing very cellular and malignant neurogenic sarcoma (Grade 3). Note mitotic figures.

A review of the eighteen favorable cases from the standpoint of the extent of disease reveals that ten of the patients were in an advanced stage of the disease. Five of these were subjected to amputation and the other five cases, all inoperable tumors, are excellent radiation results. Of the other eight cases, seven were small operable tumors cured by excision and post-operative radiation, and one was a large operable encapsulated tumor cured by excision alone. Histological examination of the tumors in the cured group was made with particular emphasis on the degree of malignancy. Fifteen sections were available for study. They were found to fall into the following groups:

Grade 1 (Acellular, fibrous)	7 cases
Grade 2 (More cellular—large spindle cells)	5 cases
Grade 3 (Highly cellular, small spindle and round cells)	3 cases
Total	15 cases

It may be seen from this grouping that the histological structure indicates

a relatively low grade of malignancy in twelve of the cured cases and a highly cellular and malignant structure in only three cases. It would seem from this data that the degree of malignancy as indicated by the cellular structure is one of the most important factors in the prognosis of the disease.

Treatment.—The ability to completely eradicate the disease by wide local excision alone is demonstrated by several cases cured by this method. It should be pointed out, however, that in these cases the tumors were encapsulated and not very cellular. These rather unique results are therefore not to be regarded as evidence against the use of radiation in the treatment of these tumors. The marked frequency of recurrences following surgical removal is largely due to the fact that the serious nature of these small movable tumors is unrecognized and the excision is not made sufficiently wide of the disease. That other factors are involved, however, is demonstrated by a number of instances in which even the wide excision of small and often encapsulated tumors is followed by prompt recurrence and pulmonary metastasis. Histological examination has shown these tumors to be of a highly cellular and malignant nature. Because of the radioresistance of these tumors it is believed that method of choice in the treatment of the operable group is surgery combined with radiation. The absolute necessity of post-operative radiation in the treatment of neurogenic sarcoma is amply demonstrated by our data. The marked tendency to recurrence, the uncertainty of complete removal, and the appearance of new tumors along the course of the same nerve in certain forms of the disease necessitate other agents as adjuvants to surgery in the prevention of recurrence and cure.

Although the principle of post-operative radiation is the same here as in other neoplastic diseases, these tumors present a peculiarly favorable setting for the employment of this agent. Many cases in which repeated excisions had been followed by prompt recurrences received post-operative radiation soon after their last excision and have remained free from recurrence for over five years.

A striking group of cases is that in which the patients, previously subjected to several operations were seen so soon after the last excision that the differentiation between post-operative reaction and local recurrence was still difficult. In some cases only a thickening in the scar was evident, whereas others presented definite recurrences. External radiation was instituted immediately. There are six cases of this type. All the patients are well and free of disease four and a half to nine years. A very suggestive feature of this group of cases in the short interval between the excision and the post-operative radiation. It is suggested that the good results obtained in this group of cases may be due largely to the promptness with which radiation was instituted. Certain theoretical consideration and histological study of radiated tissues lend support to this view. Tumor cells which have become incarcerated in strands of connective tissue in a dense post-operative scar,

are more resistant to radiation than tumor cells which are in a vascular, nonfibrous, granulating wound where the cellular reaction is pronounced and young capillaries and fibroblasts are abundant.

Based upon these observations it would seem that to be most effective against recurrence, radiation should be instituted soon after excision and the operative area radiated before formation of scar tissue. In this way foci of tumor cells are exposed to radiation when they are more radiosensitive because of a favorable tumor bed reaction. By radiating at this stage, sterilization of the operative field may perhaps be accomplished by a smaller amount of radiation than is necessary after the scar tissue formation.

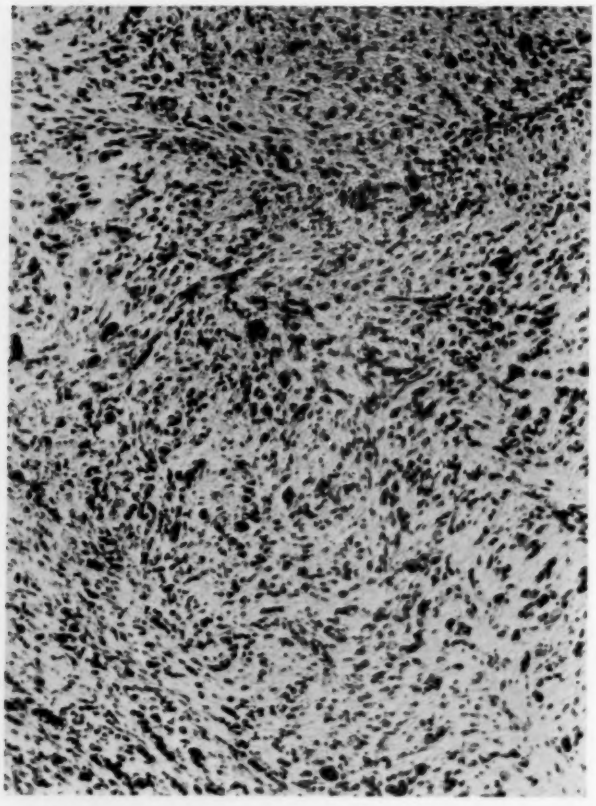

FIG. 7.—Photomicrograph showing cellular neurogenic sarcoma with giant cells of a foreign body type.

In the inoperable group, radiation has been employed in an attempt to arrest and control the disease and to relieve pain. Although many of the patients in this group succumbed to the disease, a small but definite proportion has yielded very encouraging results and demonstrate what can be accomplished even in apparently hopeless cases. Our experience in the treatment of these tumors indicates that radiation in order to be effective must be intensive. Heavy external radiation aided by interstitial radiation in selected cases are the methods that have produced the best results. By this method, alleviation of pain, regression of the tumor, and arrest of the disease may be expected in many cases and eradication of the disease and cure in a few.

In general, the plan of treatment should consider the principle that these tumors are very radioresistant and the treatment so planned as to deliver to the tumor a maximum quantity of radiation through multiple portals of entry in the skin. Rapid regression is not to be expected even after intensive radiation. Reaction to radiation may be long delayed and many months may elapse before the effects of radiation can be observed. Once regression has begun,

complete disappearance of an extensive tumor may take place as a latent radiation effect.

SUMMARY AND CONCLUSIONS

1. Based upon the belief that most of the subcutaneous and intermuscular tumors, commonly designated as fibrosarcoma, spindle-cell sarcoma, and fascial sarcoma are of neurogenic origin, all tumors presenting these features have been included under the term of neurogenic sarcoma.

2. The serious nature of these small movable subcutaneous tumors is generally unrecognized. They are commonly regarded as benign fibromas. Repeated incomplete excisions frequently result in local recurrences, in a stage of the disease in which radiation and adequate surgery would result in a cure.

3. Because of the radioresistance of neurogenic sarcoma and radiosensitivity of those tumors with which they may be confused clinically, the therapeutic test may be of practical value in the differential diagnosis. Since the method of treatment depends largely upon the nature of the tumor process, the information obtained may be of considerable value from a therapeutic standpoint.

4. Of twenty-four patients with tumors of the extremities (excluding tumors of the thigh) twelve died and twelve are alive and free of disease from three to nine years. Five of the cases are amputation cures and seven are cures affected by the conservative measures of excision or radiation, or the combined method.

5. Neurogenic sarcomas of the thigh offer a bad prognosis. Only two out of fifteen patients are alive. The structure frequently encountered in this group is myxosarcoma. The unfavorable location and the high grade of malignancy are factors accountable for the unfavorable results.

6. Ten amputations for tumors of the extremity resulted in five cures and five deaths from pulmonary metastasis. The histological structure in the amputation failures was unusually cellular and highly malignant. It is believed that the result of amputation depends upon the degree of malignancy of the tumor process rather than upon the extent of the disease.

7. Eighteen patients with neurogenic sarcoma are well and free of disease from three to nine years. Seven were small operable tumors cured by excision and post-operative radiation. Of eleven advanced tumors, five were cured by amputation, one by wide local excision and five advanced inoperable cases are excellent results obtained by intensive external and interstitial radiation.

8. Twenty per cent. are known to have developed pulmonary metastasis. The histological structure of all these tumors was highly cellular and malignant. (Grades 2 and 3.) In no case was pulmonary metastasis observed from the acellular fibrous type of growth. (Grade 1.)

9. An analysis of the failures reveals three outstanding features—the highly malignant nature of the tumor process; the advanced stage of the disease; and, the inadequacy of the treatment employed. Hence, incomplete

excision; attempted excision of inoperable tumors; and, inadequate radiation are held responsible for many of the unfavorable results.

10. Whereas wide local excision of the acellular fibrous tumors may result in a cure, this procedure is frequently followed by local recurrence and pulmonary metastasis in the highly cellular and malignant tumors. Since the degree of malignancy cannot be determined clinically, pre-operative radiation is indicated in all neurogenic tumors in an attempt to obviate the rapid recurrence following simple excision of the very malignant type.

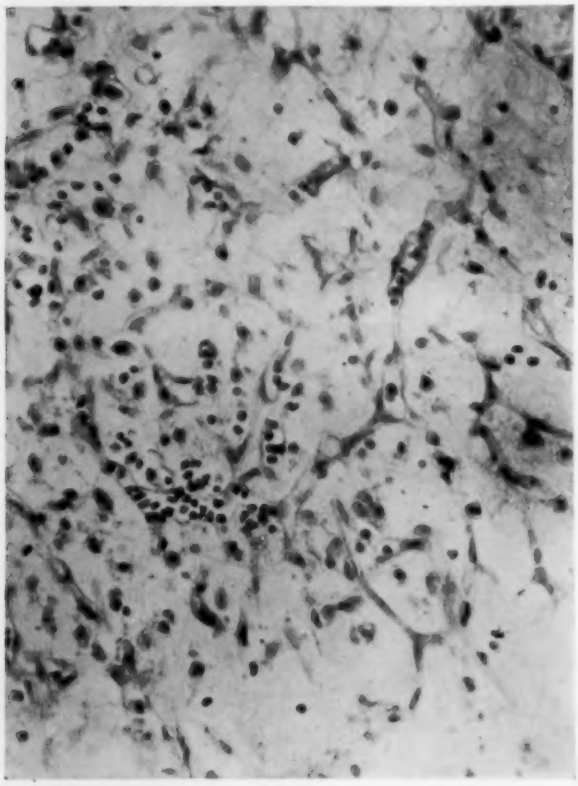

FIG. 8.—Photomicrograph showing fascial myxosarcoma. The tumor is composed of cells probably arising from the capillary endothelium and forming capillaries. The stroma is mucinous.

11. Heavy external radiation alone or combined with interstitial radiation are the methods employed in the treatment of the inoperable tumors. By this method relief of pain and arrest of the disease has been accomplished in many cases and complete cure in some.

12. Our studies indicate that pre-operative radiation followed by wide local excision and immediate post-operative radiation is the method of choice in the treatment of the distinctly operable neurogenic tumors (excluding the extremely cellular type).

13. The rapid response of a soft part subcutaneous tumor to external radiation is an indication of its highly cellular and malignant nature and a contra-indication to either interstitial radiation or surgical removal. Prolonged external radiation is the method of choice in the treatment of this type of growth.

CURED CASES

CASE I.—J. St. A., male, age forty-two, admitted October 17, 1919. Small tumor of forearm 2½ cm. in diameter removed three years before and recurred nine months later. Recurrence removed one year after first operation. Second and third operations followed by recurrences. On admission patient had a tumor 6 x 6 cm. on the flexor surface of forearm. No improvement following insertion of bare tubes. Amputation January 15, 1920. Microscopic examination revealed a large spindle-cell neurogenic sarcoma. Well seven years.

CASE II.—Male, age eleven, admitted March 10, 1921. Three soft fluctuating tumors on inner aspect of knee with complete ankylosis at the knee. Fifth recurrence. Three radium packs (24,000 mc. hrs. at 6 cm.). In September, 1921, followed in February, 1922, by amputation. Microscopic examination revealed a very cellular, small, spindle-cell neurogenic sarcoma. Well five years.

CASE III.—J. A., male, age thirty-seven, admitted February 9, 1920. Just below the knee there was an ulcerated crater 7 cm. in diameter surrounded by firm tumor tissue, third recurrence. Has had 23 X-ray treatments elsewhere. Local excision and radium pack followed by recurrence. Amputation April 28, 1920. Microscopic examination showed a large spindle-cell neurogenic sarcoma. Well seven years.

CASE IV.—A. W., male, age sixty, admitted April 10, 1920. Twenty-one excisions in past ten years followed by as many recurrences. On admission there was a small recurrence the size of a marble on the outer aspect of the humerus. Radiation, excision, zinc chloride paste, and desiccation all resulted in repeated recurrences. Amputation performed on July 15, 1921. Microscopic examination showed a large spindle-cell neurogenic sarcoma. Well six years.

CASE V.—P. C., male, age nineteen, admitted January 15, 1923. Examination showed an ulcerated recurrent tumor on outer aspect of knee (seventh recurrence). Removal with zinc chloride paste attempted but discontinued because of proximity to blood-vessels.

Amputation January 2, 1924. Microscopic examination showed a small spindle-cell neurogenic sarcoma. Well three years.

CASE VI.—F. V., male, age forty-four, admitted July 27, 1924. Small, firm, subcutaneous mass the size of a hazelnut has been present in popliteal space for many years, began to grow rapidly eighteen months ago. On examination there was a circumscribed firm nodular mass 3 x 6 x 8 cm. in the left popliteal space. Wide excision of growth on August 1, 1924. No radiation. Microscopic examination revealed a spindle-cell neurogenic sarcoma. The patient is now well and free of disease three years.

CASE VII.—F. H., female, age thirty. Admitted March 3, 1924. Primary tumor in lower abdominal wall, 3 x 4 x 5 cm., first noticed three months before admission. One low voltage X-ray exposure was followed two days later by wide local excision. The patient is well and free of disease three years. Microscopic examination showed a neuro-fibrosarcoma.

CASE VIII.—C. F., female, age thirty-eight, admitted March 20, 1920. Four months before admission, small mass which had formed in vaccination scar on arm, was removed and recurred soon afterward. Examination showed a nodular mass 2 x 2½ cm. adherent to the scar. Wide excision of mass. Base of wound treated with zinc chloride paste followed by skin graft. Microscopic examination showed a neurogenic sarcoma. Patient free of disease—six years. (No radiation.)

CASE IX.—J. I., age sixty-three, admitted January 31, 1921. Very large primary tumor occupying middle and upper thirds of humerus. Tumor measured 20 cm. in length. Biopsy specimen showed a neurogenic sarcoma. Treatment consisted of prolonged radiation with low voltage X-ray and Coley's toxins. For six months there was no change in size of tumor. Reduction in mass first noted ten months after treatment was begun. In June, 1925, cautery removal of ulcer resulting from radiation—no tumor tissue found in specimen—ulcer gradually healing. No evidence of tumor at present. Functional result good. (Radiation consisted of ten low voltage X-ray exposures given over a period of sixteen months.)

CASE X.—Female, age twenty-five, admitted April 8, 1920. Mass about size of fœtal head in right lower quadrant involving the abdominal wall extending below Poupart's ligament. At operation the tumor was found to be extraperitoneal and inoperable. Twenty-three bare tubes were distributed throughout the mass and four weeks later twenty-five more bare tubes were inserted. (Total, 4672 inches.) Heavy external

radiation was given (nine exposures within two years with radium packs; total, 74,000 mc. hrs. at 6 cm.). Biopsy specimen showed a spindle-cell neurogenic sarcoma. One year after radiation was begun there was a marked diminution in the size of the mass. Pain has been relieved, general condition of patient good. Growth arrested seven years.

CASE XI.—M. K., female, age thirty-four, admitted November 22, 1921. Large recurrent tumor of upper arm. Exploration revealed an extensive inoperable tumor infiltrating muscles. Amputation was refused. Nine bare tubes were inserted (15 millicuries), and the wound closed. Two radium packs were applied, each 8000 mc. hrs. at 6 cm. one month apart. Two years later an exploratory incision was made, but no tumor found. Coley's toxins were administered for two years. Patient is well and free from recurrence six years. Microscopic examination showed a neurogenic sarcoma.

CASE XII.—Female, age thirty-one, admitted November 10, 1922. Three and one-half years ago developed a small mass in scalp which grew rapidly. Four local excisions followed by as many recurrences. Last operation done six months before admission. Examination revealed a recurrent tumor the size of a hen's egg. At operation the main part of the mass was excised, but a small fragment of tumor adherent to the periosteum could not be removed. Post-operative radiation was instituted on the first day after operation and was continued at intervals over one month. During this period she received 60,000 mc. hrs. at 6 cm. (radium pack). The patient is well and free of disease four and a half years. Examination of the tumor showed a neurogenic sarcoma.

CASE XIII.—C. B., female, age twenty-nine, admitted December 13, 1917. Third recurrence of a tumor of the forearm removed five weeks before admission. Examination revealed œdema of the arm, but no definite recurrence. Treatment consisted of radium pack on December 17, 1917—12,150 mc. hrs. (filtration 0.5 mm. silver plus 2 mm. lead—distance 6 cm.) and five days later 3250 mc. hrs. at 6 cm. (total 21 hours). Patient is well and free of recurrence nine years. (No sections.)

CASE XIV.—H. L., male, age fifty-four, admitted November 8, 1919. Second recurrence of mass in forearm removed three weeks before admission. Has had three X-ray treatments. Examination revealed a healed six-inch scar on the dorsum of the forearm with some thickening around the scar, but no definite recurrence. Radiation consisted of six low voltage X-ray treatments given over a period of eight months. Microscopic examination of the tumor revealed a large spindle-cell sarcoma, neurogenic type. The patient is well and free of recurrence seven years.

CASE XV.—B. C., female, age forty-five, admitted September 27, 1921. A small pea-sized nodule in the outer aspect of the thigh was noticed in 1910. Five years later it began to grow rapidly and was excised two weeks before admission. On examination there was an area of thickening and induration beneath the scar 3 x 4 x 7 cm. Treatment was instituted immediately and consisted of seven low voltage and two high voltage X-ray exposures (each 80 per cent. to 90 per cent. of an erythema dose) over a period of three years. On April 12, 1922, there was no evidence of disease. On September 28, 1926, there was no evidence of disease and the skin was normal except for a telangiectasis. Pathological examination showed a cellular infiltrating sarcoma of neurogenic origin. The patient is free of disease five years.

CASE XVI.—A. L., female, age twenty-two, admitted September 14, 1922. Mass in popliteal space first noted four months ago was removed three weeks before admission. Examination revealed a firm nodular recurrence 7 x 9 cm. attached to scar in the popliteal space. Treatment consisted of heavy external and interstitial radiation with radium packs and bare tubes (total 50,000 mc. hrs. radium packs, seven exposures within three months at a distance of 6 cm.). On January 5, 1923, twenty bare tubes were inserted (total, 3300 mc. hrs.). Seven months after treatment was begun there was no evidence of the tumor in the popliteal space. Microscopic examination of the tumor showed a large spindle-cell neurogenic sarcoma. The patient is well and free of disease four and a half years.

CASE XVII.—Male, age twenty-three, admitted January 10, 1921. Two small masses present in upper abdominal wall for three years. Local excision eighteen months ago, followed by a recurrence which was removed three weeks before admission. Examination revealed a small recurrence in the scar about 2 x 3 cm. Radiation was begun three weeks after excision and consisted of three low voltage X-ray exposures (80 per cent. of an erythema dose each) given one month apart. The mass disappeared and the patient is now free of disease six years after operation. Pathological examination revealed a spindle-cell neurogenic sarcoma.

The authors are highly indebted to Dr. James Ewing who first established the disease as a clinical and pathological entity, for his invaluable aid and general supervision, without which this study would not have been possible. They also desire to express their thanks to Drs. W. S. Stone, W. B. Coley, R. Herendeen, L. F. Craver and Bradley Coley who have conducted the treatment of many of the cases for placing their material at the disposal of the writers.

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BULLET FREE IN THE SPINAL CANAL CAUSING DELAYED NEUROLOGICAL MANIFESTATIONS

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The sudden occurrence of sharp shooting pains in the legs and cramp-like abdominal pains two years after a gunshot injury is an unusual incident. In the study of this case little emphasis was, at first, placed on the bullet as a probable cause of the symptoms because the entire clinical picture was identical with that usually seen in tabetic crises. However, after more complete röntgenologic studies, the bullet was shown to be freely movable in the spinal canal. In a review of the literature it was found that foreign bodies free in the spinal canal were rarely seen; consequently this case was considered worthy of being placed on record.

Review of the Literature.—Many types of injuries to the spinal cord by bullets have been reported, but it is the purpose of this paper to review only those cases in which the bullet was freely movable in the spinal canal.

One of the earliest cases was reported by the Supervisor of the Marine Hospital[1] at Washington in 1885. The patient was a white male, twenty-six years of age, who had been shot in the back of the neck four months prior to his admission to that hospital. He had been "weak" since his injury and had had frequent mild attacks of twitching of his muscles of all parts of the body. These attacks became worse, and three weeks after admission he developed generalized convulsions. After several severe convulsions the patient died. At autopsy the coverings of the brain were congested. A .32 calibre bullet was found in the vertebral canal opposite the body of the atlas. The symptoms were caused by a gradual increase in the size of the cyst which had formed around the bullet, and death was attributed to the rupture of the cyst into the sub-arachnoid space.

In 1900, Pershing[2] gave a detailed account of a woman who had been shot in the back at the level of the eleventh rib about six inches to the left of the midline. The patient immediately became numb from the waist to the toes and was unable to move her legs. A short time later she began to have severe pains in the buttocks and lost control of her anal and vesical sphincters. The plantar reflexes, knee-jerks and Achilles reflexes were absent. The anal and perineal reflexes were active, although no sensation was present. The bullet was localized, by means of the Röntgen-rays, between the twelfth dorsal and the first lumbar vertebræ. At operation the bullet was free in the sub-arachnoid space but, due to the shift in the position of the patient, it had moved to the level of the upper part of the eleventh dorsal vertebra. Following the removal of the bullet there was no restoration of function, and the patient died three weeks later. The cause of death was not given in the report.

Loison and Mignon[4] in 1901 reported a case in which the bullet had penetrated into the sub-arachnoid space in the upper part of the lumbar region. The bullet remained free and fell to the bottom of the sub-arachnoid cul-de-sac. It was localized by means of the Röntgen-rays. At operation the bullet was not at the calculated place. Later more röntgenograms were taken and the bullet was again localized in the sub-arachnoid cul-de-sac at the level of the fourth lumbar vertebra. At the second operation the

cul-de-sac was opened but the bullet was not there. After thorough exploration with a cannula-sound the bullet was found six centimetres higher than the point of localization on the röntgenograms. This displacement was caused by the change of position of the patient prior to the operation.

Raymond and Rose,[5] in 1906, reported a case in which a bullet entered the back at the level of the second lumbar spinous process. The analysis of the symptoms and the röntgenologic examination gave the localization of the bullet at the inferior border of the third lumbar vertebra. A few weeks later the patient suddenly showed new and more severe symptoms and different localizing signs. Further röntgenograms showed the bullet at the inferior border of the first sacral vertebra. At operation the bullet was found to be freely movable in the sub-arachnoid space. After the removal of the bullet the patient recovered completely.

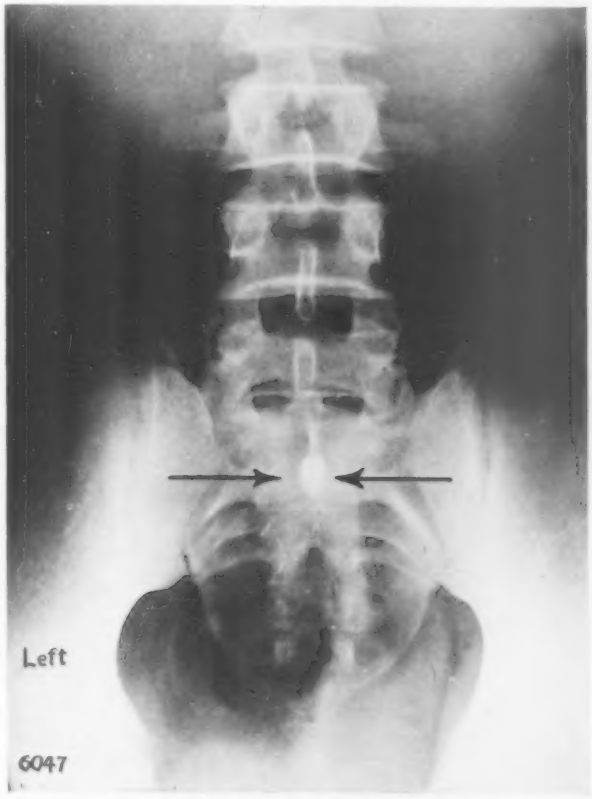

FIG. 1.—Röntgenogram showing the position of the bullet opposite the first sacral vertebra.

Bec[6] speaks of a shrapnel bullet which, by röntgenologic examination, was thought to be in the region of the second lumbar vertebra. On the basis of this examination the patient was operated upon, but the bullet was not found. Later, after numerous fluoroscopic examinations, it was demonstrated that the bullet had shifted its position in the spinal canal. At a subsequent operation it was found to be freely movable in the sub-arachnoid space. The bullet was successfully removed at this second operation, and the patient recovered.

Auvray,[8] in 1916, reported a very complete and comprehensive study of a case in which the symptoms and findings were similar to those of the case which we are reporting. At the first röntgenologic examination the bullet was thought to be in the soft tissues of the back between the spinous processes of the fifth lumbar and the first sacral vertebræ. At operation, however, it was necessary to go deeper and deeper until finally a laminectomy was necessary, since it was then decided that the bullet was probably within the spinal canal. On exposing the dura a small irregular hole was found which, apparently, was the point of entrance of the bullet. Cerebro-spinal fluid escaped freely from that opening. The dura was opened and the bullet exposed. The bullet was difficult to grasp; consequently some trauma to the roots of the cauda equina resulted. Immediately following the operation the patient began to suffer from severe pains in his legs and marked general weakness. The operator attributed this pain to the injury of the nerve roots at operation. The patient made an almost complete recovery within a year.

Bulkley and Bergamini,[13] in 1919, reported a case in which a machine-gun bullet was freely movable within the spinal canal but outside of the dura mater. At operation, while attempting to grasp and remove the bullet, it slipped and thereafter could not be found. Further fluoroscopic examinations showed that the bullet had dropped to about the middle of the sacral canal. The nose of the bullet was engaged within a small loop at the end of a wire and the missile was readily withdrawn and removed through the operative wound. The patient regained control of the vesical sphincter twenty days after the operation. There was some improvement in the motor but none in the sensory paralysis. The patient developed generalized diffuse miliary tuberculosis and died four months later.

CASE REPORT

On August 2, 1926, a colored male laborer, thirty-one years of age, entered the Lakeside Hospital complaining of sharp shooting pains in both legs, attacks of cramp-like pains in his abdomen, difficulty in walking, attacks of numbness of both legs, frequency of urination and impotence.

In July, 1923, he was accidentally shot by a .32 calibre revolver. The bullet entered the left hypochondrium near the mid-clavicular line. At that time an exploratory operation was done at a hospital in Milwaukee, but the bullet was not found. Röntgenograms taken later were said to show the bullet in the lower lumbar region. The patient made an uneventful recovery from that operation and had no further symptoms until the onset of his present illness in December, 1925.

The first attack of sharp shooting pains in his legs came on suddenly while he was resting in a chair. The pains lasted for only a few seconds. About a week later he began to have frequency of urination and difficulty in starting the urinary stream. As these symptoms became worse he began to have nocturia five to seven times each night. In January, 1926, he began to have a progressive loss of sexual power. During the following six months he had four attacks of the pains in his legs. The pains were not brought on by exercise. During the three weeks prior to his admission to this hospital he began to have frequent and severe attacks of cramp-like abdominal pain. These attacks steadily became more frequent and more severe, especially at night. There was no nausea or vomiting. During the interval between these attacks the patient was free from pain.

In 1919, he contracted an "ulcer" on his penis. His family physician gave him pills and two doses of "medicine into his arm" for that disease. Associated with the penile lesion there was a bilateral suppurative inguinal adenitis. He denied ever having had gonorrhœa. He had been married about one year, but his wife had never been pregnant.

The physical examination disclosed a robust young negro, lying on his right side with his thighs flexed on his abdomen, apparently suffering from some severe acute pain. His pupils were slightly irregular in outline but they were equal and reacted promptly to light and accommodation. The external ocular movements were normal. The eye grounds showed slight engorgement of the retinal veins, but there were no hemorrhages or areas of exudate and no evidence of choked discs. The heart was not enlarged, but there was a soft blowing systolic murmur at the apex and along the left border of the sternum. There were no diastolic murmurs. The blood-pressure was 135/85. On the anterior abdominal wall along the mid-clavicular line in the left hypochondrium, there was the scar of the previous operation. At the upper end of this scar there was another irregular scar, evidently the site where the bullet had entered the abdomen. The entire abdomen was soft and non-tender even during the attack of pains. The knee-jerks, Achilles and plantar reflexes were all absent. There were no Babinski or other pathological toe-signs present. The abdominal and cremasteric reflexes were present but very sluggish. There was no disturbance of the sense of heat, cold or pressure in the legs, but there was slight hyperæsthesia over the posterior aspect of both thighs. This

disturbance in sensation was not constant. The gait was unsteady. The Romberg test was questionably positive. There was moderate ataxia of both legs by the heel to knee test, but there was no ataxia of the arms.

Laboratory tests showed his urine to be normal on several occasions. He had 4,940,000 erythrocytes and a white blood-cell count of 7800. His blood Wassermann reaction was negative on two occasions.

Lumbar puncture yielded clear, colorless cerebro-spinal fluid under slightly increased pressure. The test for globulin was negative. There were four mononuclear leucocytes per cubic millimetre of fluid. The spinal fluid Wassermann reaction was negative. The Lange gold sol curve was normal. Three days later the lumbar puncture was repeated and the same negative results were obtained by various tests. Smears of the prostatic fluid were normal. No gonococci were found.

Röntgenologic Reports.—August 2, 1926. Films of the lumbo-sacral region in the anterio-posterior position show a metallic foreign body the shape of a bullet, at the level of the first sacral spinous process in the midline.

August 28, 1926. Fluoroscopic examination of the lumbar vertebræ, with the patient in various positions, shows the metallic foreign body at the level of the lower border of the fourth lumbar vertebra just posterior to the body of that vertebra and apparently anterior to the spinal cord.

August 30, 1926. Stereoscopic films of the lumbar spine, taken with the patient in the supine position, show the bullet at the level of the first sacral spinous process and apparently in the spinal canal. Films of the lumbo-sacral spine in the posterio-anterior and lateral positions, with the patient's pubic region elevated, show the bullet at the lower border of the third lumbar vertebra.

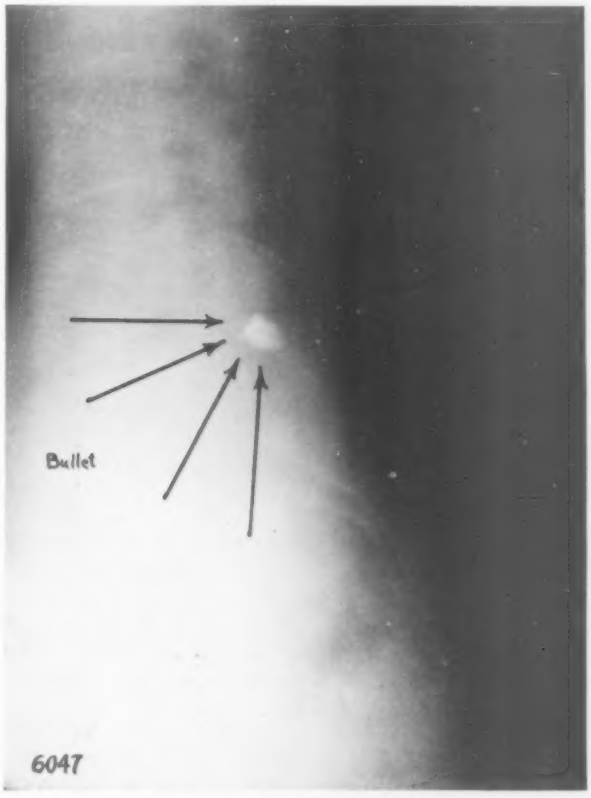

FIG. 2.—Röntgenogram with the patient in the lateral position. Arrows point to the site of the bullet.

The changes in the position of the bullet, with the patient in different positions, is to be explained by the fact that the bullet is freely movable in the spinal canal.

Operations.—At the time of the first operation at this hospital it was still thought that the bullet, which according to the röntgenograms (Figs. 1 and 2) appeared to be in the soft tissues of the back opposite the fifth lumbar spinous process, was not responsible for the patient's symptoms. In spite of this, however, it was decided to remove the bullet.

At operation the patient was placed on his abdomen and given gas-oxygen-ether anæsthesia. An incision was made just to the right of the spinous processes, extending

from the fourth lumbar vertebra to the mid-portion of the sacrum. A very careful search of this area on both sides of the spinous processes was then made but no evidence of the presence of a foreign body could be detected. A röntgenogram taken at this time showed the bullet at the lower border of the third lumbar vertebra (Fig. 3), which was much higher than the previous röntgenograms had shown it. The full significance of this shift in the position of the bullet was not appreciated at this time. The shift was attributed to the fact that the previous röntgenograms were taken in the anterio-posterior position while the reverse conditions were present when the latter röntgenogram was taken.

Since there was no evidence of a foreign body in this region outside of the spinal canal, a laminectomy was done. The laminæ of the fourth and fifth lumbar and the first sacral vertebræ were removed. The dura appeared normal throughout. Careful extradural search revealed no evidence of a foreign body. Palpation of the dura in the region exposed likewise gave no evidence of the presence of a foreign body within the dural sac. Röntgenograms were repeated, and again the bullet was shown at the level of the third lumbar vertebra. Due to the patient's condition it was thought unwise to subject him to any further exploration at this time. The wound was closed.

After the wound of the preceding operation had entirely healed, further röntgenologic studies were made. These studies consisted of stereoscopic röntgenograms and fluoroscopic examinations which definitely showed that the bullet was freely movable in the spinal canal.

Seven days after the laminectomy the wound of the previous operation was opened under novocaine anæsthesia by Dr. Claude S. Beck. This time the patient was placed in a similar position on his abdomen except that his head and shoulders were elevated by means of several pillows. The dura mater was again exposed but this time was incised. About a hundred cubic centimetres of clear, colorless cerebro-spinal fluid escaped. Soon after this loss of cerebro-spinal fluid the patient complained of very severe occipital headache. The bullet, which was free in the sub-arachnoid space, presented itself at the opening in the dura at a point opposite the middle of the fifth lumbar vertebra. In an attempt to grasp it with a forceps it readily moved upward. The patient's head was raised slightly and the bullet again presented itself in the operative field so that it could easily be removed without injuring the roots of the cauda equina. The bullet was a .32 calibre copper-jacketed revolver bullet. The opening in the dura was closed with interrupted sutures of silk. The rest of the wound was closed in layers by means of silk sutures. At the end of the operation the patient's condition was good in spite of the fact that he was suffering from a very severe occipital headache.

The patient made an uneventful recovery with a complete disappearance of all his former symptoms. During the past year he has been seen and examined at regular intervals and at no time has he had any recurrence of his former symptoms. There has been a gradual return of his sexual ability. His knee-jerks and Achilles reflexes are still very sluggish, but at present no other neurological disturbances can be demonstrated.

Discussion.—After reviewing the cases already reported, it is fair to conclude that the presence of a foreign body in the spinal canal is of grave significance. Hughes,[10] in his conclusions based on five cases where the missile lay in the spinal canal, states that opening the dura admits such a great additional risk that the indications must be very definite to justify it. His experience, as well as the experience of Guillain and Barré,[11] tends to show that in the cases which recover from injuries of the spinal cord, caused by bullets, the spicule of bone from the fractured vertebra, or the bullet, does not penetrate into the sub-arachnoid space but causes the symptoms by pressure on the cord from outside of the dura mater. This, however, has not

been true in the majority of the cases reported in the literature nor in the results in our own case. Hull [7] cautions about the early removal of foreign bodies from within the dura because of the dangers of infection of the spinal meninges. He advocates allowing sufficient time to elapse in order that the individual may overcome any low grade infection in the wound.

The violent headaches which follow such an operation as opening the dura mater may be a rather serious complication. The severity of the headache can sometimes be lessened by placing the patient flatly on the back and elevating the foot of the bed. Hypodermoclysis and external heat may also be of some benefit. Weed and McKibben,[13] Leriche [14] and others advocate the use of intravenous injections of distilled water in doses of forty cubic centimetres in all cases where there has been a marked loss of cerebrospinal fluid. This is usually effective in diminishing the severity of the headache even when it is of such an intensity that complete abolition is practically impossible.

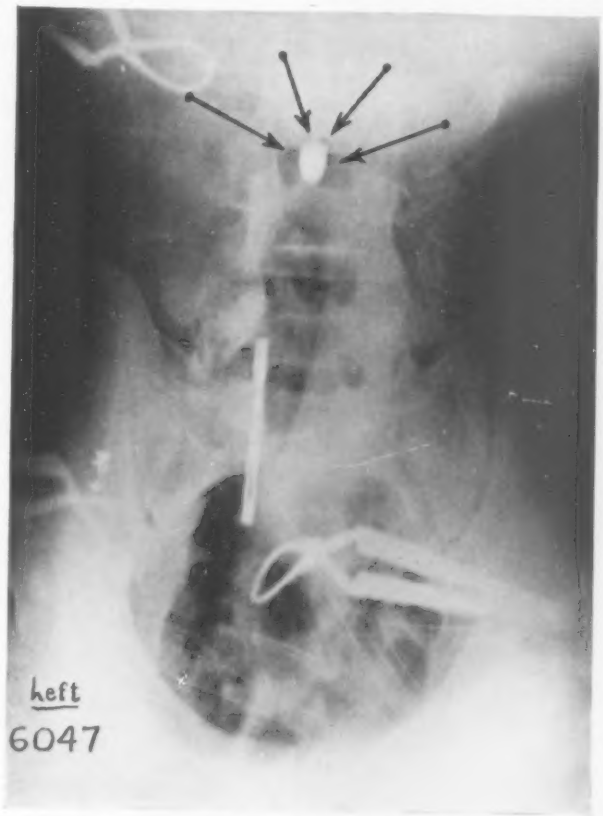

FIG. 3.—Röntgenogram taken at the time of the first operation. The bullet is shown at the lower border of the third lumbar vertebra.

In any case of a foreign body in the region of the spinal column it is very important to have the röntgenograms taken with the patient in various positions. Fluoroscopic examinations, as well as stereoscopic röntgenograms, of doubtful cases are usually of great help in making an accurate localization of a foreign body. It has been the experience of those who have reported similar cases, that, unless careful röntgenologic studies have been made before the first operation, the attempt to find the foreign body may be unsuccessful.

It is difficult, in the case reported here, to explain the sudden onset of the severe paroxysms of pain. Probably the bullet had been held by one of the spinal nerve roots or by a reflection of the spinal meninges and suddenly became dislodged in such a way as to remain free in the sub-arachnoid space.

Its subsequent movement in the sub-arachnoid space would cause irritation to the roots of the cauda equina and in that way produce the severe paroxysms of pain. The patient was unable to associate the onset of the initial attack of pain with any sudden trauma.

SUMMARY AND CONCLUSIONS

1. A foreign body free in the spinal canal is rarely seen.

2. The symptoms caused by a foreign body free in the spinal canal may closely resemble those usually seen in tabetic crises.

3. The majority of cases that have been reported have been subjected to more than one operation because the foreign body was not at the point originally localized by the Röntgen-ray examination.

4. Elevation of the patient's head and shoulders may be sufficient to bring the movable foreign body into the operative field.

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THE END RESULT IN ALBEE'S OPERATION FOR SPLINTING VERTEBRÆ

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The accidental discovery of an old Albee splinting of the vertebral column in one of the bodies delivered to us for dissection affords the opportunity of studying the end-result of this operation.

The cadaver is a white male, ca. fifty-five years of age. The cause of death was chronic mania: there is no clinical history. Existing sinuses in right Scarpa's triangle and about the upper right tibia assure us of mixed infections starting with bone tuberculosis. The fused condition of the twelfth thoracic and first lumbar bodies with evidence of old damage through loss of substance with partial collapse of ventral parts suggests strongly a healed tuberculous lesion.

The condition which called for the operation is of no significant interest, except insofar as it might modify the normal healing of bone after surgical interference. That no such modification has occurred is sufficiently obvious and we may therefore dismiss the question which resolves itself into mere academic speculation.

Fig. 1.—Upper left tibia showing source of splint. The area whence the splint was removed, broader below than above, is healed and the excavation almost filled up with new bone.

Since there is effective and complete fusion of the articular processes also it may be inquired whether, as might quite likely be the case, a Hibbs' operation has been performed also. There is no indication of mutilation or operative interference in these articular processes and, judging from other cases of vertebral pathology, their fusion need not have been definitely provided for by a kind of erosion of the articular surfaces.

The figure of the left tibia shows that a splint 117 mm. long and somewhat broader below than above, has been raised from the upper subcutaneous surface. Healing of the tibial wound has taken place perfectly and the trench left by operation in the shaft has practically filled with new bone.

The splint, now 75 mm. long, has been dovetailed into the spinous processes of the twelfth thoracic and first lumbar vertebræ, its broader part above. The narrow end of the splint projects below the spine of the first lumbar but did not reach the spine of the second which was not grooved to receive it. Perfect healing of the splint in its new environment has resulted in the fusion desired by the operator.

FIG. 2.—Dorsal aspect of splinted vertebræ. The splint lies in a groove cut in the spinous processes of the twelfth thoracic and first lumbar vertebræ. Perfect union has taken place between spinous processes and splint and elsewhere the latter presents a typical passive appearance.

Important light is thrown upon the controversial question whether the splint actually remains or simply acts as a temporary scaffolding for new bone which ultimately replaces it. This is the question which also arises regarding fossils, in which problem the true answer invokes at times one, at times the other of these two replies, and sometimes indeed involves both. Texture is an infallible guide to bone history (see Todd, T. W. and Iler, H. D., "The Early Phenomena of Repair in Bone," 1927, ANNALS OF SURGERY, vol. lxxxvi, p. 715).

A smooth waxy texture is characteristic of bone which has lost its periosteum, has been largely reduced in its blood supply and hence has lost the power of adding to its substance. Fragments falling into this category frequently occur in compound simple fractures. Their vitality is diminished but not destroyed. They take no active part in regeneration but do contribute their strength and rigidity to the new bony mass in which they find themselves incorporated. Of such texture is this splint where it has been lying surrounded by soft tissues between the two splinted spinous processes and extending downward therefrom. The remarkable thing is that such a bone though becoming a foreign body in the midst of soft tissues, suffers no erosion and is not absorbed though it may be bent as this one is. But above all it does not die: it is merely passive.

A quite different result is apparent in the areas of the spinous processes. Here the splint shows traces of an original erosion of surface, rarefaction of adjacent substance and marginal proliferation (external callus), processes which have also involved the neighboring parts of the spines, so that fusion of the splint in place is perfect and the united areas have become quiescent long ago. The original splint has undergone the same transformation in these sites as any active fragment undergoes in the repair of a fracture, neither more nor less. It is quite erroneous to hold that the splint is not permanent and is replaced by new bony issue. But it is equally erroneous to refuse to admit the marked marginal modifications which are inseparable from the repair processes inducing fusion.

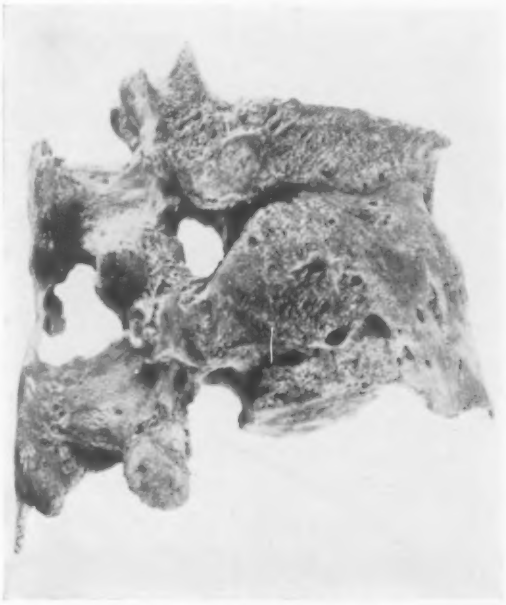

FIG. 3.—Right side of splinted vertebræ. Note the union of bodies and articular processes, the bending of the splint and the waxy texture of passive bone.

SUMMARY

The case is one of perfect functional result from an Albee's operation uncomplicated by any Hibbs' procedure.

Where the splint is grafted into the spinous processes there has been marginal erosion and proliferation of new bone precisely as in the repair of a fracture.

Where the splint lies embedded in soft tissues no proliferation or change has taken place in the implanted bone, except that a modification of its texture has occurred indicating a living but inactive condition.

Hence both current views are justified regarding the fate of the splint, namely, that it remains unchanged and also that it acts as a temporary scaffolding for the erection upon it of new bone tissue.

CHANGES IN BLOOD CONCENTRATION WITH SPECIAL REFERENCE TO THE TREATMENT OF EXTENSIVE SUPERFICIAL BURNS*

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Among the nutritional requirements of the body that of water holds a prominent place. Normally, the capacity of the organism for storing water is very great. The body usually possesses an available store of water which exists for the most part in the muscles and skin although all tissues undoubtedly share in this function. When for any reason water is withheld or withdrawn from the body the different tissues and organs vary markedly in their water loss. Thus, the fatty tissues, the brain, heart, and bony structures lose relatively little water as compared with the muscles and skin. More than one-half of the water lost is given up by the muscles without apparent injury to either structure or function. The same is probably true for the skin.

On the other hand in water loss the condition in the blood is quite different. It is an axiom in physiology that the composition of the blood is constant. Comprehended in this statement is the recognition of small fluctuations in either direction induced probably by the organism in its attempt to maintain the equilibrium of the circulating medium. Under normal circumstances the stability of blood composition is remarkable. This constancy of blood composition may be regarded as one of the most fundamental requirements of the organism in its endeavor to safeguard the environment of the cell. As proof of the general proposition just cited one has only to think of the constancy of blood sugar content, of the urea of the blood, of uric acid, of the stability of the acid-base equilibrium, and of the small variations in inorganic constituents, as calcium, magnesium, sodium and potassium.

Attention, however, is particularly called to an entirely different aspect of blood composition. Normally, the water content of the blood constitutes one of the body's constants. Attempts to alter the water content of the blood by introduction of even large volumes of fluid have failed to change appreciably blood composition. The water regulating mechanism is adequate to make the proper compensation quickly. It is only when this mechanism is overwhelmed either experimentally or as a result of disease that marked changes in blood concentration occur. Either dilution or concentration effects may then be observed, although, in general, from studies thus far carried through concentration is more commonly encountered than is dilution.

* The substance of this communication formed the basis of an address before the New York Section of The American Chemical Society, June 3, 1927.

The literature on the subject of blood concentration has been reviewed under the title of Anhydremia by Marriott W. McKim: Physiol. Reviews, 1923, vol. ii, p. 275.

In the blood, concentration to even a moderate degree results in recognizable symptoms. The first indication noted is impairment of the circulation. When water loss becomes great the circulatory deficiency is magnified. The thick, sticky blood finds difficulty in its passage through the capillaries. It becomes an inefficient oxygen carrier, resulting in partial asphyxiation of the tissues. In consequence, there may be alteration in the metabolic processes, and when blood concentration has reached a certain high level a disturbance in the heat-regulating mechanism occurs: the temperature, at first, elevated, falls and vital activities are suspended.

Before discussing further the problem of blood concentration it may not be out of place to consider the question how to measure changes in blood concentration. Of all the constituents of the blood only the red corpuscle fails to pass rapidly through the capillary wall. From this viewpoint it would appear that the measurement of hæmoglobin content should serve as an excellent indicator of changes in blood concentration. This procedure, however, is not entirely free from possible sources of error since in various diseased conditions it is well recognized that hæmoglobin content varies greatly especially over extended periods of time. Moreover, even in short time intervals new corpuscles may be poured into the blood stream or masses of corpuscles may be held in certain restricted areas. Again, "when a condition of severe anhydremia has lasted for a number of days a decrease in the concentration of hæmoglobin and of serum protein occurs even though the body weight and the blood volume determinations may indicate a further loss of water (Lust, Marriott). This may be taken as indication of destruction of blood corpuscles and of serum protein. The experiments of Gürber on frogs, of Utheim on rabbits and Keith on dehydrated dogs shows a decrease in the total number of red blood cells in the circulation, when the diminished total blood volume is considered in connection with the cell counts and protein concentration. As a result of this destruction of the blood constituents an abnormally low cell count, hæmoglobin and serum protein contents of the blood are often observed following a restoration of the blood volume of fluid administration. It is thus seen that determination of the cell count, hæmoglobin or serum protein may at times fail to indicate accurately the degree of anhydremia. The same may be said of the determination of total solids. The measurement of blood volume taken together with the determination of the other constituents mentioned supplies the necessary data for the estimation of the degree of anhydremia."

On the other hand, where it is desired to follow changes in blood concentration at frequent intervals the usual blood volume methods are inadequate or too cumbersome to fulfill the experimental conditions. A consideration of this problem over a period of years has convinced the writer that for the purpose of observing blood concentration changes during short intervals of time the hæmoglobin method is unsurpassed by any other method yet proposed, provided experimental conditions are adequately controlled, that small fluctua-

tions are disregarded, and that due consideration is given to possible changes in the number of red corpuscles.

Clinically, severe blood concentration may be encountered when water is refused for prolonged periods as exemplified in cases of mental derangement. Individuals exposed to the high heat of the desert or subjected to the heat of boiler rooms or mines (Haldane) often show marked blood concentration. Vomiting induced by any cause may be productive of severe blood concentration. This is especially true for infants with pyloric stenosis since little water is absorbed from the stomach and relatively little reaches below the pylorus. High intestinal obstruction leads to the same result.

In persistent diarrhœa much water may be lost to the organism through the stools. In Asiatic Cholera and certain forms of diarrhœas in infants such loss is peculiarly marked and may be productive of blood concentration to a degree sufficient to lead to death. In infants especially severe blood concentration is likely to occur, partly, from the fact that they have a high water requirement which may not be covered since they are dependent upon others for their water supply, and, partly, for the reason that infection may induce refusal of food, vomiting and diarrhœa with a subsequent concentration of the blood. In cases of infantile toxemias, so-called, it is generally exceedingly difficult to determine whether concentrated blood initiates the clinical symptoms or whether concentrated blood must be regarded as secondary to some other change in metabolic processes. Certain it is, however, that in many of these cases if blood concentration can be restored to the normal level the condition of the infant is usually greatly improved and soon regains the normal state.

It is well recognized that in war gas poisoning the outstanding feature of the pathological state is the markedly concentrated blood. In certain fulminating cases of influenza a similar condition is presented and in extensive superficial burns concentrated blood may be chiefly responsible for the clinical symptoms evoked. In eclampsia and in surgical shock the blood is generally concentrated above the normal level.

Experimentally a concentrated blood may be induced by restriction of water intake, by sweating, by the action of certain drugs, as pilocarpine, cantharides, saline cathartics, by proteose, histamine, by administration of sodium chloride or urea by mouth or by the intravenous injection of sodium chloride, urea, glucose, saccharose or lactose.

The composition of the blood when highly concentrated shows various changes such as increased viscosity, and the non-protein nitrogen is generally augmented which may be explained in part by the functional disturbance of the kidney induced by the dehydrated blood and in part by an increased destruction of protein. Sugar of the blood may also be above normal. This finding is a common occurrence in other conditions associated with a lowered blood volume as in shock (Cannon). It may also be induced under a variety of circumstances in which there is vaso-constriction or a diminution in the oxygen-carrying capacity of the blood (Araki). Acidosis, as indicated by

diminished alkali reserve, carbon dioxide content and bicarbonate combining power, is a prominent feature of a highly concentrated blood, which, however, rapidly disappears when the blood volume is restored to the normal level. Acidosis therefore must be regarded as a secondary manifestation induced without doubt by the failure of the circulation. When the kidneys are affected acid phosphates may be retained which is undoubtedly an additional factor in the production of acidosis.

With a highly concentrated blood there may be evidence of a distinctly impaired functional capacity of the kidney. The kidney only occasionally shows structural changes. All evidence of renal impairment disappears with the restoration of a normal water balance. This fact leads to the conclusion that the renal insufficiency is purely functional, probably the result of the inability of the kidney to separate a normal urine from a concentrated blood.

The blood pressure may be high or low; usually, however, it is well maintained. In shock, of course, and in Asiatic Cholera it may be very low. One reason why dehydration of the blood does not cause a significant fall of pressure is perhaps because the increased viscosity prevents that condition which might be expected to occur with a decreased blood volume.

In most of the published discussions relative to changes in blood concentration apparently little attempt has been made to differentiate these changes and correlate them with the types of reactions calling them forth. For example, in conditions of clinical anhydremia no distinction is made between the state existing in water starvation and that induced by extensive superficial burns and yet there must be a vast difference in the significance to be attached to the two conditions. This is especially prominent when attempts are made to restore the blood to a normal level of concentration. In the case of anhydremia induced by water deprivation simple administration of water rapidly restores the blood to its normal condition whereas in anhydremia from superficial burns the restoration to normal is much more difficult. It would appear that in the two examples cited fundamental differences exist in the mechanism leading to the anhydremia. There are at least two ways in which blood concentration may be induced. In the first place one may imagine that a fluid, nearly simple water, or a dilute salt solution, in composition, leaves the blood-vessels in response to the proper stimulus, resulting in a more concentrated blood, a dehydration, a desiccation as it were. Or again by a different type of mechanism, or perhaps as a result of a different form of stimulus, fluid of the nature of dilute plasma rather than of salt solution passes through the vessels leaving behind a blood concentrated above normal. That both these two types of change occur will be pointed out later.

The impetus for our own studies in changes in blood concentration came from experience with war gas poisoning in which it was shown that the intensive irritation of the respiratory tract by the gas called forth a massive œdema which is associated with very marked blood concentration. The intensity of blood concentration under these circumstances became so great that the heart was unable to push the thick viscid blood through the capillaries at a rate

sufficient to aerate properly the tissues, resulting eventually in tissue asphyxiation, fall of temperature, circulatory failure, and death. Death was ascribed to the change in blood concentration rather than to pulmonary œdema. From a wide experience the impression was gained that within certain well defined limits concentrated blood, although not compatible with proper nutrition, is not necessarily a serious condition. Beyond these limits, however, life can be maintained for only a short interval. To put it differently—blood concentration up to 125 per cent. of the normal value is not serious but when 140 per cent. has been reached danger enters and life is not possible for long if this limit is maintained. These relatively wide variations which may occur without serious consequences may be regarded as another example of the factors of safety resident in the organism. That death is due to blood concentration rather than to pulmonary œdema can be tested experimentally by gassing two animals with the same concentration of gas for equal periods of time. Both animals will develop pulmonary œdema to the same degree and both will present the same blood concentration picture. If one is treated so as to maintain blood concentration below the danger level recovery will follow, whereas the untreated animal will die. In neither case does the treatment materially change the lung condition, at least during the critical period.

Another striking example of this type of blood change is seen in certain cases of influenza, the alteration of concentration of the blood being invariably associated with a fatal outcome. From the standpoint of pathology these cases of influenza present a lung picture difficulty distinguishable from that of gas poisoning. From these two facts, together with the similarity in the manner of death, one may be perhaps warranted in concluding that the mechanism called into play in the two instances is either the same or else closely related.

It seems a far cry from gas poisoning and influenza to superficial burns and yet in the latter instance the blood may be markedly concentrated and if sufficiently so undoubtedly plays a large contributing rôle to a fatal outcome. The proof for this statement lies in the fact that if by any means blood concentration can be prevented or abolished the chances of recovery in any of the conditions cited are very materially increased.

Our experience with the treatment of the systemic effects of superficial burns was gained as a result of observations carried through on more than twenty victims of a theatre fire in New Haven.

The patients were admitted into the New Haven Hospital † in the early evening and at once received first aid treatment and were sent to the various wards. Blood concentration estimations were made at once. From the clinical standpoint the patients were divided into two groups (*a*) those seriously burned (*b*) those not so seriously burned. The blood concentration of the first group was above the danger level, namely, more than 125 per cent. Those

† Through the courtesy of Dr. Samuel C. Harvey, Surgeon-in-Chief in the New Haven Hospital, opportunity was afforded to us to conduct this investigation. (The details of the work are published in the Archives of Internal Medicine, 1923, vol. xxxii, p. 31.)

less seriously burned were below this level. The correspondence between the severity of the clinical picture and the blood concentration was perfect. In the first group all patients were placed upon the danger list, in the second none were included in this list. The first point of significance in this investigation is that the determination of blood concentration which takes only a few moments serves as an indication of the gravity of the patients' condition and also points out definitely the type of treatment necessary.

In our opinion the serious condition in burn cases is the concentration of the blood and treatment should be directed to reduce this concentrated blood to a more fluid state. The systematic treatment of these burn cases consisted simply in the forcing of fluids, water by mouth when possible, when the patient could not coöperate because of unconsciousness, fluid was injected under the skin, directly into the blood, by the rectum, etc. The quantity of fluid taken in varied from four to eight litres daily.

In a day or two on this treatment the blood concentration fell gradually and the patients' condition steadily improved. All patients so treated recovered although of the group of those severely burned the vast majority could be regarded as poor risks.

"Although from figures and other data relative to these observations one is apparently justified in concluding that restoration of blood concentration is of prime significance in burn cases, nevertheless, to the sceptically inclined there are at least two points at which the above conclusions may be attacked. In the first place, one may assume that fluid intake has only an inappreciable influence on blood concentration, that fluid is excreted from the body almost as rapidly as it is ingested. All the available literature on the subject supports such an assumption. One point, however, must be emphasized, namely, that in nearly all instances in which this hypothesis has been put to the test the organism employed was that of a normal person. Herein lies the crux of the whole matter. It is utterly fallacious to predict the behavior toward water administration of an organism suffering from lack of water from observations made on an organism with a sufficiency of water supply. It is quite true that partaking of large volumes of water by normal man or dog does not perceptibly alter the concentration of the blood. So long as the water regulating mechanism of the body is normal such a result is to be expected. On the other hand, when an animal has been deprived of water for a sufficiently long period, blood concentration becomes markedly increased. Water administered under these circumstances causes a rapid fall in the concentration of the blood. The experiments by Keith and by Underhill and Kapsinow cause us to reiterate the statement previously made that it is fallacious to draw conclusions relative to the abnormal organism when these inferences are largely based on observations on normal persons, and they furthermore dispose of one of the points of attack cited above.

A second point of attack centres in the query, "Did the fluid intake in these cases actually influence blood concentration or would blood concentration have returned to the normal without such aid?" To answer this question

absolutely control experiments would be necessary. Such a control, however, is obviously lacking. The question receives a partial answer from the experiments of Keith and our own cited above together with our experience with war gas poisoning. Death may follow, but blood concentration is not restored to near normal limits under conditions of water lack unless sufficient fluid has been introduced. We believe, however, that the question is fully answered by our experience with one burned patient treated outside the hospital. A victim of the same fire, this patient was cared for at his home by his own physician. Special attention to forcing of fluids was lacking. This case was especially badly burned and presented the typical signs and symptoms characteristic of intoxication from burns, chief among which was an active delirium, it being necessary to take measures to keep the patient in bed. This was succeeded by a period of collapse and unconsciousness, death being anticipated. After a period of eight days, consultation with the physician resulted in the active forcing of fluids. Previous to fluid administration (two litres of 0.7 per cent. sodium chloride solution subcutaneously) the hæmoglobin value was 163 per cent. A few hours after the salt solution had been given the patient regained consciousness, became rational, and was capable of coöperation in taking of fluid. Blood concentration fell rapidly and the patient went on to recovery. The point to be emphasized here is that this patient on the eighth day after being burned still had a blood concentration equal to that in some of our own serious cases on the first day. The presumption is valid that if this patient's blood concentration would have returned to normal of itself it should have done so within a period of eight days, an interval during which none of our own treated patients maintained such a concentration.

From such data it would appear that water intake is responsible for the decrease in blood concentration observed in our cases, and it is quite safe to assert that without such water introduction blood concentration would not have taken the decided fall observed in every case. We believe, therefore, that the observations recorded justify the conclusion that water introduction in sufficient quantities to restore blood concentration to within normal limits is of paramount importance in the treatment of burned cases. As a result of this type of treatment, it may be stated that only two patients gave any evidences of symptoms characteristic of intoxication in burns. In these cases unconsciousness at first prevailed; this, however, disappeared after restoration of the normal blood concentration. In all the other cases, the patients presented no untoward symptoms, such as delirium, unconsciousness, gastro-intestinal disturbance, hæmoglobinuria, albuminuria, etc. Whether such facts are to be interpreted from the viewpoint that restoration of blood concentration prevented the development of conditions responsible for these symptoms or that fluid introduction caused prompt elimination of toxic material so diluted as to be innocuous or both, remains a problem the solution of which can be determined only in the future. At any rate, from either viewpoint it would appear that fluid introduction is a rational method of treatment for extensive superficial burns."

Since the initial experience gained from the victims of the theatre fire we have had occasion to treat a number of burned cases in the New Haven Hospital and have been consulted on cases in various parts of the United States and in general the results obtained from the treatment have been very encouraging.

How is it that the same type of mechanism is called into play in two such diverse pathological conditions as war gas poisoning and superficial burns? A little thought will show that the difference is apparent rather than real—the seat of action is the factor which makes the apparent diversity.

In a consideration of the development of pulmonary œdema in gas poisoning I wrote the following—" the lethal war gases are all substances eminently irritant to living tissues and it must be accepted that the irritation produced by a gas is the initial step in the development of œdema. In response to the first irritative stimulus tissue fluid finds its way to the injured area in an apparent attempt toward repair or alleviation of the injury. It is conceivable that if damage to the tissue is only slight such a procedure would result in the passage to the damaged area of only a small quantity of tissue fluid. According to this view the degree of response with respect to the local deposition of tissue fluid would be in direct ratio to the extent of injury. On the other hand, it is equally plausible to assume that this reaction may reach a breaking point at a certain degree of stimulation whereby the whole mechanism governing the exudation of tissue fluid is thrown out of control so that the response to the stimulation becomes overwhelming. Under these conditions a reaction which in its initial function may be regarded as beneficent eventually becomes a direct menace to continued existence on the part of the mechanism as a whole, merely by interposing difficulties in the way of respiration and circulation." If in this quotation one substituted for war gases, heat as the irritative stimulus playing upon the skin the mechanism is entirely similar. With burns, fluid rushes to the skin, resulting, if the skin is unbroken, in either œdema of the part affected or blisters; or if the burn is more severe fluid drips from the raw surfaces. Our experience in burned cases leads one to believe that the quantity of fluid lost in this way during the first few hours after the injury may be very large, in fact sufficiently great to account for the rapid blood concentration which occurs.

Other abnormal conditions which produce a marked concentration of the blood are Asiatic Cholera; shock, whether arising spontaneously from trauma or toxemia, or evoked experimentally by peptone or histamine; dysentery; acute arsenic poisoning and peritonitis.

If one analyzes these pathological states it must be quite evident, that the one underlying factor common to all with the exception of shock, is that an extensive inflammatory reaction is prominent, acting usually upon a more or less restricted area, as the respiratory tract, the skin, the alimentary canal, the peritoneum, etc. All are areas plentifully supplied with capillaries.

In order to understand the nature of the mechanism producing the blood concentration a word as to the character of the fluid lost from the blood is

essential. From my own observations on gas poisoning it becomes apparent that this fluid partakes of the nature of plasma, diluted plasma, as it were, containing somewhat less protein than plasma, but otherwise of practically the same composition. The fact that significant quantities of proteins are present and indeed the blood proteins, particularly fibrinogen, leads to the view that the irritant factor has changed the character of the capillary wall. In ultimate analysis therefore one may conclude that the direct cause of blood concentration, in the pathological states under discussion, is due to a changed permeability of the capillary wall.

In most of these instances actual loss of fluid to the body has occurred sufficient in amount to account for the concentration of the blood. With shock, however, where no loss of fluid to the body takes place the explanation of the mechanism is not so obvious. Under shock conditions increased capillary permeability may also explain the mechanism involved since the fluid leaving the vessels is plasma (Bayliss, Dale). The toxic substance responsible for the condition acts more or less specifically upon the capillaries resulting in a pouring of fluid into the tissue spaces of the body, thus provoking an exceedingly rapid and marked blood concentration.

From our experience and conception of the mechanism involved in the loss of plasma from the blood a change in capillary permeability is essential—in the loss of salt solution no such alteration is necessary. We believe that any irritative or inflammatory reaction upon any extensive area of mucous membrane may, if sufficiently acute, cause a rapid loss of plasma resulting in blood concentration. In general it is this type of blood concentration which is likely to prove disastrous to the organism. We shall return to this point later.

Blood concentration induced by loss of water and presumably salts only, results in a concentration by a process of dehydration or real desiccation. This is what occurs when sufficient fluid is not introduced as by experimental water deprivation of animals, or clinically in the dehydration of infants. Again intense secretion induced by pilocarpine or purgation by the saline cathartics will cause a rapid blood concentration. It is significant, however, that this process in general does not proceed to the point where a dangerous degree of blood concentration is attained. The concentration approaches the danger line but is not maintained. This, however, is only a general statement and is particularly applicable to the saline cathartics and to pilocarpine. If actual water deprivation is pushed for a sufficiently long period blood concentration steadily mounts and death follows. Such a result, however, can be called forth only by drastic measures.

Blood concentration of this type is obviously of an entirely different nature than that induced by an inflammatory reaction. This becomes quite apparent when attempts are made to restore the blood to its normal concentration. In the former case administration of fluid is all that is essential. With the concentration induced by an inflammatory reaction administration of fluid alone although helpful is not strikingly successful. Why? Because in the latter instance the capillary wall has been modified so that it is no longer

capable to the normal extent of retaining fluid. In other words, in the one type of blood concentration the capillary wall is involved, in the other it is not, at least to an extent capable of measurement.

The potency of the agencies which may play upon the mechanism governing blood concentration are determined in large measure by the fluid content of the body at a given moment. Thus, when an animal has been deprived of water to the point where blood concentration becomes significant even though still within safe limits, the saline purgatives no longer cause purgation. With sodium sulphate and Rochelle Salts no immediate symptoms are in evidence. When magnesium sulphate is employed complete anæsthesia takes places and unless treatment is given immediately death follows. This fact may have a certain clinical bearing in the indiscriminate use of Epsom Salts both before and after operation. The administration of plenty of fluid both before and after operations is in most instances a wise procedure. From this viewpoint if a cathartic is to be used it should be one which by its action does not draw fluid from the blood.

It is also quite probable that shock may be much more easily produced in an organism in which the blood is concentrated than in one when the fluid reserves are normal, for in peptone shock the blood concentration curve is distinctly modified and the poison appears to be more potent.

Another point of considerable clinical significance is the fact that it is much easier to prevent marked blood concentration than it is to change it once it has become established. For the prevention of blood concentration large volumes of fluid are essential administered more or less continuously. In certain instances venesection tends to keep down concentration acting as it were as a stimulus upon the reserves of the body to maintain constancy of blood concentration. In attempts of the past to maintain blood concentration the error in procedure has been that only a single intravenous infusion has been made or repeated infusions at infrequent intervals. The relief afforded has been only temporary since the fluid quickly left the vessels. Administration of fluid should be more or less continuous and it is essential only to attempt to reduce the concentration to the safe limits. This reduction of concentration by administration of fluid or by venesection plus fluid need be practiced for relatively short periods only—it carries the individual over a critical period—a period necessary for restoration of the normal permeability of the capillary wall—in other words the capillary wall repairs itself which takes from twenty-four to forty-eight hours. It is during this period that fluid must be pushed continuously.

In the treatment of burns, therefore, the essential object is to keep the blood concentration near a normal level until the blood capillaries in the skin injured by the heat have had an opportunity to repair themselves and again become capable of holding within themselves the fluid of the blood in a normal manner.

A NEW EXPLANATION OF THE IMPROVED RESULTS FOLLOWING LIGATION OF BOTH ARTERY AND VEIN

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Within the last ten years the point of view regarding operations for arterial ligation has changed. Formerly all operative procedures were directed to preservation of the accompanying vein. This was done not only to avoid hemorrhage but also to preserve the venous circulation intact. As a result of the experience in the World War it was held that this was an erroneous opinion and that simultaneous ligation of artery and vein should be done. This procedure was suggested by Sehrt[10] and Propping[9] in Germany, Kendal[7] in Tuffier[11] and Makins[8] in France, and England. It is due to the efforts of Makins that this principle has become so well founded. The investigations of Halsted,[3] Brooks,[1] Holman,[6] Heidrich,[4] and Drummond[2] substantiate the contention that balancing the circulation is desirable. Thus, there is both clinical and experimental proof of the fact that simultaneous ligation of an artery and its companion vein diminishes gangrene and improves function. The

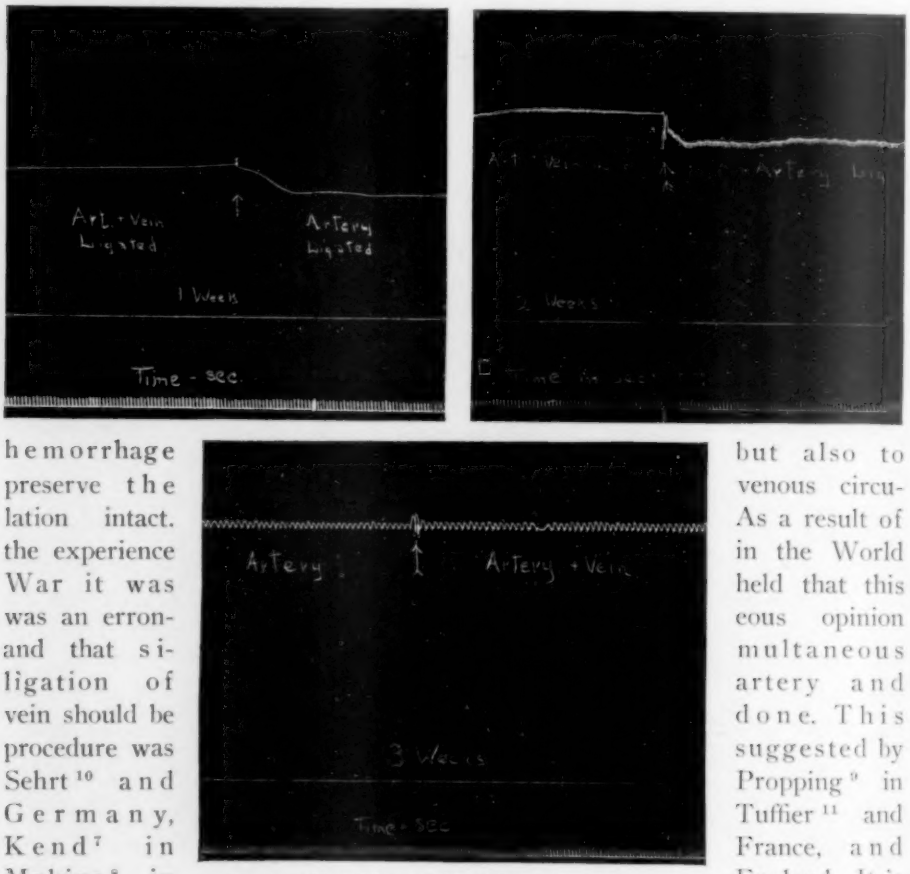

Fig. 1.—The difference in residuary blood pressure in animals having the femoral artery and the femoral artery and vein ligated. *A*. One week after operation. *B*. Two weeks after operation. *C*. Three weeks after operation.

explanation of this phenomenon is not clear. Kend [7] first showed that the residuary arterial blood pressure is elevated by ligation of the vein. This has been confirmed by subsequent investigators. Brooks [1] observed that the temperature of the extremity falls at the time of ligation of the vein. He also demonstrated a greater increase in venous pressure than in arterial pressure and interprets these findings to mean a diminution in the volume flow of blood through the extremity. Holman,[6] on the other hand, by direct methods, found that the volume flow after arterial ligation was doubled by ligation of the vein at the same level. It is to be noted that these findings have been obtained only in sacrifice experiments of a few hours' duration. The vagaries of small fluctuations in blood pressure are well known. It appears that these explanations alone are insufficient. It was considered that, since gangrene and functional disability are sequellæ of the operation, it was not proper to explain their absence on results obtained at the time of the operative procedure. Consequently, animals were operated upon and allowed to survive so that at intervals they might be studied. It was found that the elevation in residuary blood pressure and increase in blood flow were but transient phenomena and that perhaps the fundamental cause of the diminished gangrene and improved function after ligation of artery and vein was marked increase in the arterial vascular bed.

FIG. 2.—The vascular bed two weeks after ligation of the artery and vein (on the side with the marker) compared with that after ligation of the artery alone.

Method.—Adult cats were used. Under ether anæsthesia a low midline skin incision, extending 1 cm. below the symphysis pubis was made. By lateral traction the femoral vessels were exposed. If it was desired to ligate the common iliac vein the rectus muscle was split, but the peritoneum was not opened. By blunt dissection the peritoneum was lifted up, from the lateral

wall of the pelvis and the common iliac vein exposed by this extra-peritoneal method. All experiments were done under conditions of surgical asepsis and the animals permitted to survive.

The operative procedure was of three types:

(1) The femoral artery and femoral artery and vein of the opposite side, were all ligated at the same level.

(2) Both femoral arteries were ligated and the common iliac vein of one side was occluded.

(3) The femoral artery and vein of one side were ligated. On the opposite side the femoral artery and the common iliac vein were tied.

This allows comparison in an animal of the effect of

(1) Ligation of artery and vein versus artery alone.

(2) Ligation of the vein proximal to the site of ligation of the artery, according to Holman's [6] principle, versus ligation of the artery alone.

(3) Ligation according to Holman's procedure, versus ligation of the artery and vein at the same level.

At intervals of one to three weeks after operation the animals were studied.

When the blood pressure and minute volume flow were to be compared after different operative procedures, they were always obtained from the femoral arteries of the same animal. The apparatus was arranged so that readings could be made on either side by merely turning a valve. These results obtained with cats were verified on dogs to assure the corrections of the findings.

The circulatory bed was visualized by röntgenograms after arterial injection with Hill's [5] opaque mass.

Results.—The average increase in residuary arterial pressure caused by ligation of the vein is 11 mm. Hg. If the pressure is obtained one week after ligation the average increase is found to be 8 mm. Hg. In two weeks the difference is less marked and was never more than 4 mm. Hg. In some of the animals tested two weeks after operation the pressures on the two sides had completely equalized. At the end of three weeks there was no instance of a difference in arterial pressure after ligation of vein and artery, as compared with occlusion of the artery alone. Typical tracings of these results are shown in Fig. 1. Ligation of the vein proximal to the site of ligation of the artery results in a more marked elevation of the residuary pressure, but even after this procedure the pressures have equalized in three weeks. Arterial pressures were not observed in those animals in which Holman's procedure was compared with the older method of ligation at the same level.

The arterial tree in the operated extremities was visualized by röntgenograms taken one, two, or three weeks after operation. The maximum change was usually obtained at the end of two weeks. It was found that the vascular bed in the limb having artery and vein ligated was much richer than in the limb having only the artery occluded. This is shown in Fig. 2. Holman has advocated ligation of the vein proximal to the point of ligation of the artery since he has found that this gives better results. From the experiments here

presented it was considered that this procedure resulted in a better vascular bed than did ligation of the artery and vein at the same level. In order to eliminate individual variations the two methods were compared on the limbs of the same animal. In every instance it was found that the circulatory bed was increased on the side having a proximal ligation of the vein. This is illustrated by Fig. 3 where it will be seen that, though the contrast is not marked yet, an apparent difference is present.

Discussion.—The present investigation has demonstrated that the increase in residuary arterial blood pressure following ligation of the companion vein is only a transient phenomenon. It is greatest at the time of operation. At the end of one week it has diminished, but there is present a well marked difference in the limb having both artery and vein occluded. In two weeks the difference between the limbs is less or may be absent. Finally by the end of three weeks pressures on two sides have equalized. It was considered that the minute volume flow of blood from divided artery fluctuated directly with the arterial blood pressure.

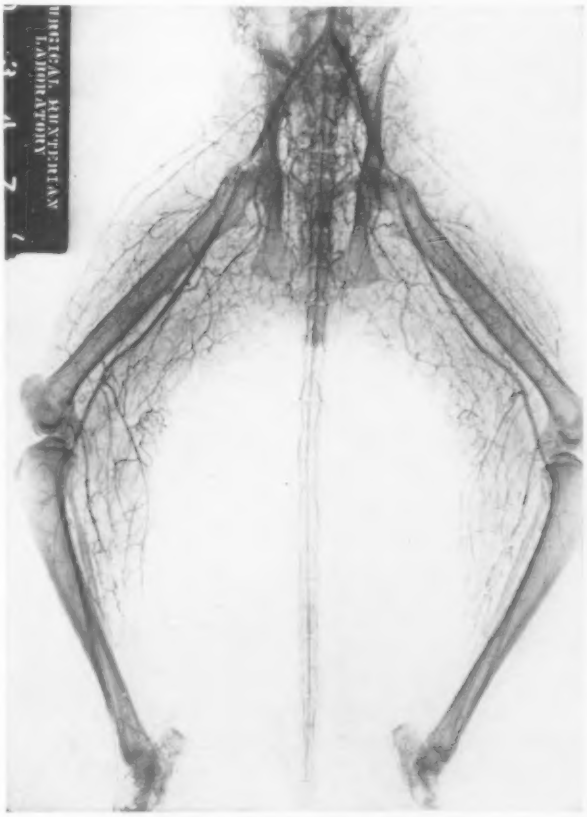

FIG. 3.—The arterial circulation with ligation of artery and vein according to Holman's principle (on the side with the marker) and ligation of the artery and vein at the same level.

It has been shown that after ligation of artery and vein the distal circulatory bed is much greater than after occlusion of the artery alone. This is considered to be the fundamental explanation of the improved function and diminished gangrene seen after ligation of both the artery and vein. It has been observed, also, that ligation of the vein proximal to the site of ligation of the artery according to Holman's principle results in a better vascular bed than does any other procedure.

The fallacy of explaining a delayed result on an immediate finding is obvious. It is not the increase in arterial pressure resulting from vein ligation that improves the results, since at the time one judges the results the arterial pressures have equalized. Rather, it is considered the fact that simultaneous

ligation of artery and vein results in an increased arterial vascular bed. The part played by the increased arterial pressure in producing this latter phenomena cannot be estimated. It is probable that it is one factor in its causation.

SUMMARY

(1) Ligation of a large artery should be accompanied by ligation of its companion vein. This results in improved function and diminished gangrene.

(2) The increased arterial pressure and blood volume flow observed in sacrifice experiments at the time of ligation of the vein are but transient phenomena.

(3) Survival experiments have demonstrated that ligation of the artery and vein results in a much richer vascular bed than that occurring after ligation of the artery alone.

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CHRONIC POST-OPERATIVE TETANY

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The incidence of toxic goitre has increased rapidly in this country during the last decade in spite of the efforts that have been made for its prevention. Our knowledge concerning the etiology of this disease remains obscure, but there has been a marked advance in diagnosis and treatment. Statistics have demonstrated beyond a doubt that the early intervention by surgery in cases of toxic goitre is for the most part attended with success. The remarkable reduction in mortality after operation is due to the development of medical science and to the fact that patients are coming to operation sooner because of correct diagnosis. The perfection of the basal metabolic unit as an aid to clinical diagnosis, and the discovery of the efficacy of iodine as an aid to surgery in the treatment of exophthalmic goitre, have greatly aided in the successful treatment of this disease.

That the goitre question is one of interest to the medical profession is apparent from a survey of the literature. There is a goitre clinic in the majority of large cities and the number of patients coming to operation has rapidly increased in recent years. Through dissemination of knowledge of the end results of toxic goitre the incidence of cases of chronic myocarditis should decrease and the surgical mortality should decrease still further. With the greatly increased number of operations, however, an increase in surgical complications may likewise be expected. Because of the close proximity of the goitre to so many vital structures, the removal of this gland is always attended with a certain degree of risk. Injury to the recurrent laryngeal nerve, collapse of the trachea, hemorrhage, embolism, tetany, pneumonia, and tracheitis are only some of the possible complications that may develop after thyroidectomy. Fortunately these are not of common occurrence, and yet there is scarcely a surgeon who has not experienced one, or all of them.

The surgeon, in discussing the successful results of operation, may have a tendency to minimize the complications, and it is with the hope of stimulating further interest in the subject that I present the problem of tetany as a complication of thyroidectomy. This was a serious problem for those who first operated on goitre and in the clinics of Billroth and Kocher, it resulted in a high mortality. As surgeons became better acquainted with the condition they became more conservative, so that for many years the operation of choice was simple lobectomy. The end results of this operation likewise proved disappointing; it resulted frequently in incomplete cure or recurrence. Gradually the operation of resection as suggested by Mikulicz came into vogue. Frequently recurrences were still observed until within recent years

surgeons have learned that for successful results it is necessary to remove all but a small portion of the gland. If too much tissue is removed, injury to the recurrent laryngeal nerve may occur or tetany develop. Recurrence may follow the failure to remove enough of the gland. Although these complications are the exception, they occur even after most careful surgical technic.

Reports of post-operative tetany are numerous in the literature, but the statistical study of a group of cases has not been presented.

Structure and Function of Parathyroid Glands.—Post-operative tetany was first recognized by Wölfler in Billroth's Clinic in 1881. A year before this the first description of the parathyroid glands (thyroid glandules, epithelial bodies) was made by Sandström. These glands arise from the walls of the third and fourth bronchial clefts. They may vary in number and situation. Usually there are four and they are situated in pairs along the posterior surface of the thyroid, the superior at the upper pole and the inferior at the lower pole of the gland. According to MacCallum [15] they have no constant position and may appear singly or in groups; they may be on the surface or imbedded. They are in close relationship to the superior and inferior thyroid arteries, and according to Halsted and Evans receive their principal blood supply from the latter; they also receive some from anastomosing branches between the two. They are brown and soft, showing peripheral veins, and are formed of strands of cells, many of which have clear protoplasm in early youth, while in later life the predominant cells have a slightly granular cytoplasm, a few groups standing out by reason of their small dark nuclei and the bright eosinophile protoplasm.[16] The function of these cells has not been determined.

The literature concerning the parathyroid glands contains little of importance from the time of Sandström's exposition until 1891, when Gley rediscovered these glands. He felt that they were embryologically and physiologically related to the thyroid gland, and that when the latter was removed its duties were assumed by the parathyroid glands. Both Sandström and Gley felt that these glands were embryonic thyroid tissue which possessed the power of replacing the thyroid.

It remained for Vassale and Generali to disprove completely this theory and to establish the separate relationship of these glands. They were able to produce fatal tetany in animals by the removal of the parathyroid glands while preserving the thyroid. Tetany was prevented by preserving the parathyroid glands in spite of complete thyroidectomy.

The next advancement in our knowledge of the parathyroid glands was made by MacCallum and Vogel. These workers showed that the hyperexcitability of the nervous system is peripheral and is the result of an alteration in the blood. They were able to produce marked stimulation of the nerves by introducing blood from an animal with tetany into a normal animal. Further study of the blood from an animal suffering with tetany showed a low calcium content. MacCallum and Voegtlin, together with Parhon and

Urechie, independently arrived at the same conclusion, that calcium is beneficial in cases of parathyroid tetany. They showed that this condition could be relieved by the use of a 5 per cent. solution of calcium lactate or acetate, orally or intravenously. Magnesium salts were found to be objectionable on account of their toxicity, while the administration of potassium salts intensified the symptoms.

That hydrochloric acid as well as calcium will relieve tetany in dogs was made known by Wilson, Stearns, and Janney in 1915. In their experiments with animals they found that the muscular contractions that occur in cases of tetany are apparently a compensatory effort on the part of the body. Alkalosis may occur but this is neutralized by the acid which is produced by the muscular contractions. Acidosis then develops and the tetany subsides. These interesting phenomena suggest further fields of study.

Paton and Findlay in studying the blood and urine of parathyroidectomized dogs found that guanidin and methylguanidin were present in considerably larger amounts than in normal animals. The same condition was found to exist in children with tetany. These findings apparently suggest some relationship between the two forms of tetany, but as yet there is no pathologic evidence to substantiate this.

In 1918, Howland and Marriott determined that the blood calcium in the serum of normal persons varies between 9.2 and 11.3 mg. (about 10 mg.) for each 100 c.c. of serum. The calcium in the serum of patients suffering from idiopathic tetany was reduced to an average of 5.6 mg. for each 100 c.c. of serum. They believed that convulsions develop if the blood calcium content becomes less than 7.0 mg. for each 100 c.c. This test has proved of great practical value and now governs the rationale of therapy.

Many preparations of parathyroid gland have been tried in the treatment of tetany, but none proved of value until in 1924, Collip found a parathyroid hormone which will prevent or control parathyroid tetany and regulate the level of blood calcium. He was able to show a marked rise in blood calcium content after injections of his extract in both normal and parathyroidectomized animals. Several reports have appeared in the literature in which this preparation has proved of definite benefit in the treatment of cases of tetany, and I am reporting three cases in which parathormone was administered (Cases II, III and V).

Etiology of Tetany.—Surgeons have generally agreed that only a small portion of gland along the posterior border should be preserved if thyroidectomy is to prove successful in patients with exophthalmic goitre. Preservation of too much gland results in only partial abatement of the disease or definite recurrence with exaggeration of symptoms. To protect the recurrent laryngeal nerves, the parathyroid glands, and the trachea, and yet remove sufficient thyroid gland, the operation must be carefully performed. The tendency to remove more and more tissue has perhaps accounted for increase in the incidence of tetany. On account of the minuteness of the parathyroid

glands and their close resemblance to the surrounding tissue it is difficult to detect them during operation. I believe it is impossible to demonstrate their presence when operating for adenomatous goitre because of the similarity of small adenomas to the parathyroid gland. Consequently the surgeon must be guided by anatomical relations and endeavor to preserve these small bodies by avoiding rather than seeking them. In removing adenomatous goitre the operator may realize that he is resecting more of the gland than desired, because in its degenerated condition the tissue seems to disappear before the knife. It may still be possible to preserve sufficient tissue to prevent injury to the parathyroid glands. Undoubtedly tetany in some cases is not the result of direct injury to the glands, but rather to a cutting off of their blood supply either through ligation of the vessels, or from œdema and scar tissue. It may be also that tetany is present in a potential state before operation. Herrick recently reported that he was able to demonstrate clinical signs of tetany in certain cases of goitre preceding operation. A patient with a large adenomatous goitre on whom I recently operated had for three years had typical tetany-like cramps in the hands and feet as well as the epigastrium. Definite clinical signs of tetany could not be elicited, however, and the amount of blood calcium was normal. Still it does not seem impossible that the rapid growth of a goitre might not cause some pressure atrophy of the parathyroid glands.

Symptoms.—The classical signs of tetany, best known by the names of those who first described them, need only to be mentioned. In 1851, Trousseau demonstrated that in the free intervals between spasms, attacks could be induced by exerting pressure over the main nerve trunk of the forearm either with the hands or a tourniquet. This is not easily obtained and in my experience is neither as simple or as satisfactory as Chvostek's sign. Chvostek, in 1907, found that by gently tapping along the course of the facial nerve, the muscles could be made to twitch so that the corner of the mouth or the ala of the nose is slightly drawn. In 1874, Erb showed that the electric excitability of the motor nerves is increased. This was clearly demonstrated in my Case V when a slight current caused my fingers merely to twitch, while it produced a violent contraction of the patient's entire body. Pool, in 1907, and Schlesinger, in 1910, produced contracture in the legs of patients with tetany by flexing the leg on the body, thus obtaining tension of the sciatic nerve.

Other signs have been described but none of these compares in value to that of determining the calcium in the blood; this portrays accurately the patient's condition.

There may be an acute onset of symptoms of post-operative tetany within twelve hours; it may be delayed for two or three days, or it may develop chronically after an interval of several months as in Case III. Boothby states that prodromal symptoms such as headache and general weakness, accompanied by radiating pains down the extremities, especially the upper, and

chronic twitchings may occur. Only one of my patients complained of headache, but fleeting pains in the arms were mentioned by every patient. They all complained of stiffness in the hands and feet with a sensation of numbness and tingling as described by patients suffering from pernicious anæmia. A tentative diagnosis was made at this stage in two cases and treatment with calcium was begun. Coincident with the stiffness of the fingers, the face becomes stiff and drawn and soon a corner of the mouth may be definitely pulled to one side. Spasms develop in the hands and often in the feet. The hands may assume the typical contraction of the accoucheur's hand, the fingers flexed at the metacarpophalangeal joint, the hand flexed at the wrist, the thumb adducted, and the arm flexed at the elbow. These spasms may subside in a few minutes only to recur again soon. They may gradually become less severe, or they may progress to a fatal termination if the proper treatment is not instituted.

Treatment.—In my experience calcium administered either orally or intravenously has proved entirely satisfactory in controlling the attacks of tetany in all but one case. In this case Collip's parathormone injected intravenously proved most beneficial. In the five chronic cases reported here neither of these remedies effected cure.

In my cases of acute tetany a blood calcium test is made at the onset of prodromal symptoms. Calcium lactate is then given orally, three doses of 120 grains each at one-hour intervals. In case the symptoms do not subside, three additional doses are administered. Further treatment is based on the progress of the case and the laboratory data. In the mild transient cases I have observed, this amount of calcium has usually been sufficient to tide the patient over the period of temporary hypoparathyroidism. It may be necessary to decrease the doses gradually for several days.

Ten cubic centimetres of 5 per cent. solution of calcium lactate given in 100 c.c. of sodium chloride solution produces almost immediate relief in the more severe cases of tetany; the spasms subside and the other symptoms usually disappear in from ten to thirty minutes. Calcium lactate may still be given by mouth or by rectum, but in the transient acute cases one intravenous treatment will usually suffice.

The cause of this acute temporary form of tetany is not known. It has been supposed that there is a disturbance of the blood or the nerve supply of the parathyroid glands due to trauma or œdema. Possibly there is a destruction of one or more of the glands, and until those remaining can compensate, there is a period during which the parathyroid glands are unable to function properly. In cases in which the condition persists for several weeks and then clears, it may possibly be relieved by the establishment of collateral circulation. These cases need cause little concern; the real problem is what to do in case of chronic tetany. The symptoms in the five cases in my series have persisted two years from the time of operation. As long as calcium lactate is given orally in daily doses the condition is perfectly con-

trolled, as is myxœdema by thyroid feeding. The question is, must these patients continue taking calcium lactate indefinitely or is there some means of permanent relief?

Transplantation of the parathyroid glands has been advocated and tried by various surgeons since 1912, when Halsted reported a successful result in an experiment on a dog. Crotti states that if a parathyroid gland be inadvertently removed during an operation, it must be reimplanted at once in the thyroid tissue. He believes that the chances for this autotransplantation are very good. Theoretically this is plausible, but practically the question is whether or not, at the completion of an operation, a parathyroid gland has been damaged or removed? It is almost impossible to recognize the gland macroscopically in the midst of adenomatous tissue.

Crotti believes in regard to heterotransplantation that "in the majority of these cases this method has proved a failure. Its effects, as a rule, are only temporary and last only during the time necessary for the graft to become absorbed." If a parathyroid gland is to be transplanted Crotti states, and justly so, that the gland should not be removed from a normal patient. Kocher removed a gland from a person who had committed suicide, and Pool from a person who had died from a non-communicable disease. In such cases no effect of the graft may be expected for one or two months. The rectus muscle is the favorite site for transplantation.

Lahey recently reported that in a period of six months he transplanted parathyroid glands into the belly of the sterno-cleido-mastoid muscle in ten cases. Later twenty-six additional supposedly parathyroid glands were transplanted, but a microscopic examination showed that only four of these were actually proven to have been parathyroid glands, two were questionable and nineteen were probably lymph-glands. Lahey admits the difficulty of recognizing parathyroid glands macroscopically and states that a microscopic study should be made.

Transplantation of glands has in general, however, proved unsatisfactory and consequently the report by Collip on a parathyroid hormone was received with interest.

Parathyroid Hormone.—Collip stated that the function of the hormone in the normal animal appears to be that of a regulator of calcium metabolism and its action is primarily that of mobilizing calcium. It has been shown that parathyroid hormone relieves or prevents tetany when it is injected into parathyroidectomized animals. The injection of the hormone in both normal and parathyroidectomized dogs causes a definite mobilization of calcium in the blood stream. Collip warns against the danger of injecting excessive amounts of hormone and producing hypercalcæmia. This procedure should not be carried out unless blood calcium values are determined. In the animal the condition is evidenced by a great increase in inorganic phosphorus in both the whole blood and serum, an increase in urea and non-protein nitrogen, and a great increase in viscosity accompanied by a decrease in plasma

volume. Anuria occurs and later acidosis. No fatal cases of hypercalcæmia in man following this treatment have been reported in the literature.

In one of my cases of tetany relief following the administration of parathormone was more prompt and beneficial than that obtained by the use of calcium, but the patient was not cured. However, Collip did not maintain that permanent relief would follow.

Snell [27] reported a case of chronic tetany in which the administration of calcium lactate brought about some improvement in the clinical condition, but did not raise the blood calcium. When parathormone was given with the calcium lactate, the blood calcium rose to normal, and all signs and symptoms of tetany disappeared. In a later report, however, he stated that the patient is now taking daily 15 gm. of calcium lactate and no parathormone.[28] He pointed out that in spite of the fact that the calcium metabolism was defective for a long time, normal blood calcium cannot be maintained by calcium alone. It was impossible to do this in the early treatment of the case until a course of parathormone had been given.

Lisser and Shepardson reported a case of post-operative tetany in which three parathyroid glands had been removed; the tetany was relieved by the administration of from 12.5 to 50 units of parathormone daily. Some symptoms of hypercalcæmia were observed. Later 5 gm. of calcium was given daily.

Lilly's parathormone is standardized by its capacity to increase the total calcium in the blood serum of normal dogs. One unit may be defined as one-hundredth the amount of extract required to cause an increase of 5 mg. of calcium in the blood serum of a dog weighing 20 kg., the rise of calcium being determined fifteen hours after the injection of the extract. Parathormone (Lilly) is supplied in 5-c.c. rubber-capped ampules. Each ampule contains 100 units and is designated as P-20, which indicates that there are 20 units in each cubic centimetre.

John recently reported interesting data and observations on his experience with parathormone in cases of chronic tetany. The conclusion that he deducted from the literature as well as his own experiments was that parathyroprival tetany is due to a disturbance of the mechanism which governs the metabolism of calcium. The essential element for the operation of this mechanism is supplied by parathormone. In his cases of chronic tetany a serum calcium content of not less than 8 mg. for each 100 c.c. was observed. He found that after the use of parathormone the symptoms of tetany are relieved and the calcium in the blood rises. A similar rise in the serum calcium content, together with a reaction, was seen after parathormone was given to normal persons. He believes that there is a psychological factor of tetany because relief was obtained in certain cases by only normal sodium chloride solution.

In my own experience with parathormone, which has been limited to three cases of chronic tetany, I found that this preparation was most valuable

in restoring temporarily the normal blood calcium (Case V). At the present time these patients are all taking calcium lactate by mouth; blood calcium is maintained at normal values and there are no symptoms of tetany.

Ultra-violet Light.—The favorable effect produced in cases of rickets in animals from treatment by ultra-violet light suggested this method to me as a means of treating cases of chronic tetany. One of my patients (Case V) had been receiving 600 grains of calcium lactate by mouth in daily doses for almost two years. On several occasions she had neglected treatment, so that twice it was necessary to administer calcium lactate intravenously to relieve acute exacerbations. At other times tetany was purposely induced so that parathormone might be administered: When there were no symptoms of tetany and the blood calcium was 9.5 mg. for each 100 c.c. of blood the dosage of calcium by mouth was reduced one-half. At the same time treatment with ultra-violet light was begun. In three days the blood calcium had fallen to 7.56 mg. and early signs of tetany were observed. The treatment with ultra-violet light was increased four minutes a day and no more calcium lactate was given. Five days later the blood calcium had risen to 9.15 mg., and all symptoms of tetany had disappeared. The condition continued to improve so that one month after treatment was instituted the blood calcium was 10.5 mg., that is, 1 mg. more than when treatment was begun. On the patient's return two weeks later the blood calcium was 10.8 mg. and she felt well. The dosage of calcium was again reduced one-half, this time with no visible effect. At this time she was receiving ultra-violet light treatments, thirty minutes daily. The dose of calcium has been reduced to one-eighth the original dosage, to approximately 75 grains a day. The patient has remained well and has received no ultra-violet light treatment for more than two months.

Deductions may not be made from a single case. The effect of the ultra-violet light may be merely transient and palliative. In view of the ever-increasing number of cases of chronic tetany now being reported, I believe this preliminary report may aid others to try this method and increase our knowledge in this difficult field.

After I had carried out this work I found in the literature a report on the subject by Grant and Gates. They performed experiments to determine the effect of ultra-violet light on the parathyroid glands of the rabbit, and found that exposure of the skin to a quartz mercury arc lamp, thirty minutes daily, caused a marked increase in the weight of these glands. This increase, which was 56 per cent. of the normal weight, began during the first few days of exposure. It was more remarkable in that it occurred during a period when the glands were normally undergoing an apparently seasonal diminution in weight. In working with normal animals it was found that hypertrophy of the parathyroid did not result with a corresponding increase in the calcium content of the blood when the calcium concentration was already at, or near, the normal level. Grant and Gates felt that one of the results of exposure

of the skin to ultra-violet light was slight alteration in the composition of the blood. The parathyroid glands are sensitive to this, and their reaction is to hypertrophy.

Salvesen injected calcium lactate into dogs after removing the parathyroid glands and he observed a temporary increase in the blood calcium, which he felt was due to a rapid elimination, for the most part through the intestines, of the calcium which had been injected.

Orr, Holt, Wilkins, and Boone found, in cases of active rickets in children, when there is very little retention of calcium in the body and the blood calcium values are low, that exposure to ultra-violet light caused greatly increased retention of calcium and phosphorus.

These experiments suggested to me the problem of determining the effect of the ultra-violet light on the calcium metabolism of parathyroidectomized animals. Swingle and Rhinhold found that there was no change in the calcium content of the blood serum after animals with tetany had been treated by ultra-violet light. They were able, however, greatly to prolong the life of these animals and to modify the symptoms. I believe this matter should receive further study.

John, in a report on chronic tetany, presented the chart of a patient who had received two treatments of ultra-violet light without apparent effect. He did not discuss the subject, although he mentioned the work of Denis and Corley, who found that daily exposure to ultra-violet light had no effect on the calcium content of the tissues or serum. Here again, however, as in the experiments of Grant and Gates, the studies were made on normal animals.

Diet.—Luckhardt emphasized the importance of prescribing a diet with a high calcium content; this includes milk, peas, beans, eggs, and sauerkraut. In his early investigation which he made with Rosenbloom he found that the poison responsible for tetany is of exogenous origin, and that it is found particularly in meat. They were able, by feeding meat to an animal to precipitate an almost fatal attack of tetany thirty-three days after parathyroidectomy. It was found important to prevent constipation. They were able to keep parathyroidectomized animals alive by the intravenous injection of Ringer's solution and after about forty days no symptoms of tetany were noted.

REPORT OF CASES

Case I.—A woman, aged thirty-six, who came to the Clinic December 1, 1924, with severe exophthalmic goitre, had taken iodine at home for the last year. She had lost 50 pounds. The loss in quadriceps was graded 4, and the basal metabolic rate was +49. She had chronic myocarditis, œdema of the legs, and mitral insufficiency. The case was considered only a fair surgical risk, and the usual pre-operative treatment was instituted.

December 11, primary thyroidectomy was performed. There was partial resection of the right lobe, isthmus, and left lobe. One-fourth of a normal lobe on the right and one-third on the left were preserved. Convalescence was uneventful. The patient left the hospital on the fourth day and on the following day she came to the Clinic

for a dressing. On January 2, 1925, she was ready to make the journey home but complained of stiffness and contractions in the hands. Two grains of thyroid extract and 10 grains of calcium lactate were given three times daily. January 7, there was no improvement. One-tenth grain parathyroid extract was given three times daily in addition to the thyroid extract and calcium lactate. The basal metabolic rate was +20. The patient had gained 7 pounds. January 17, there was no relief and the patient had another attack of cramps; 4 gm. of a 10 per cent. solution of calcium lactate was given every three hours during an attack, and she was dismissed from observation.

The patient wrote in a letter of May 11 that she had been having mild attacks of cramps three or four times a week. She now complains of a severe rheumatic pain

FIG. 1.—Case of chronic post-operative tetany. Note the muscular contraction of the face and hands.

in the left forearm and hand that is not relieved by calcium lactate. She returned to the Clinic May 20, and was examined for tetany. The blood calcium was 8 mg. for each 100 c.c. of blood serum; 50 grains of calcium lactate was given three times daily and the patient received a full milk diet. The basal metabolic rate was +4. On May 23, a Röntgen-ray examination revealed periostitis of the median third of the mesial aspect of the ulna. No relief of the pain could be obtained by giving calcium even when it was administered intravenously. On June 8, tonsillectomy was performed. December 4, the patient stated in a letter that she had gained 40 pounds, was free from all symptoms, and five months' pregnant. I received indirect information that she died at the time of childbirth, but I was unable to ascertain whether or not tetany was a factor.

CASE II.—A woman, aged fifty, came to the Clinic January 17, 1925, because of multiple non-toxic substernal adenoma of the thyroid. Her chief complaint was dyspnœa. Clinical examination revealed an unusually hard nodular gland, suggesting a calcareous or possible malignant change. At operation the left lobe was found to be hard, and suggested calcareous change throughout. A portion two-thirds the size of the normal lobe was preserved on both sides as usual. The inferior thyroid arteries were not separately ligated. Eighteen hours after operation the patient complained of numbness and stiffness

in the hands and a drawn feeling in the face; she seemed nervous and apprehensive. The house physician, suspecting the development of tetany found that the calcium content of the blood was 10 mg. for each 100 c.c. The symptoms progressed in spite of the administration of 30 grains of a 10 per cent. solution of calcium lactate three times daily. During a mild attack the calcium content fell to 7 mg. for each 100 c.c. and during a severe attack it was only 4 mg. Almost instant relief was obtained by the intravenous administration of calcium chloride and milk was found beneficial (Fig. 1).

February 19 the patient reported that during the two weeks she had been home she had suffered one severe attack of cramps and one mild one. She was taking 30 grains of calcium lactate three times daily. The basal metabolic rate was +9. On April 6, she was free from tetany. On May 26, she reported that she had had occasional mild cramps each week or two, but was much better, especially when she abstained from eating meat. More than a year later she was still having occasional mild cramps; June 3, 1926, she had a more severe attack and the family physician gave a larger dose of calcium lactate with relief. The next day she had 5 units of parathormone. The calcium lactate was increased to 50 grains, three times daily, together with 10 grains calcium carbonate. This was suggested to aid in the absorption of lactate. June 18, the cramps had subsided but treatment was continued and the patient has remained free from symptoms. The blood calcium was 9.6 mg. for each 100 c.c. If I had known what I do at the present time, I should have given a larger dose of calcium lactate at the start and more parathormone.

Case III.—A woman, aged forty-eight, came to the Clinic, April 21, 1925, because of exophthalmic goitre. This was a severe case and is the most unusual and remarkable instance of tetany that I know. The patient had passed through two gastro-intestinal crises during the last year; each time she was confined to bed for many weeks. When she was first seen she was on the verge of a third crisis. She had been in bed much of the time for several months. The response to treatment was rapid and on May 3, primary thyroidectomy was performed. There was nothing unusual about the operation or the pathologic findings. The gland was very friable and vascular showing some reversion to colloid. The usual strip of gland along the posterior border was preserved. Convalescence was uneventful and the patient was dismissed from observation May 23, twenty days after operation. The basal metabolic rate was +1, and the weight 148 pounds. June 19, she came for three physiotherapy treatments and was gaining rapidly. December 4, she weighed 190 pounds, the pulse rate was 72, and she was considered cured. January 9, 1926 she weighed 220 pounds, having gained rapidly during the last ten months. She had become childish; her voice was deep; there was some dryness and scaling of the skin; the ankles were swollen; the abdomen was bloated, and the region under the eyes was puffy. She suffered from the cold. The responses were quick; there was no loss of hair; there was a strong suggestion of myxœdema, but the case was atypical and the basal metabolic rate was 0. In spite of this, 10 mg. of thyroxin was given March 13, with no apparent improvement.

Because six weeks previously the patient had fallen and struck her head, had lost consciousness, and blood had run from the ears, the possibility of a fracture of the skull was considered. The röntgenogram revealed no evidence of fracture. The depth of the arterial sulci indicated intracranial pressure. The attacks since this accident suggested petit mal.

When the patient was admitted to hospital her condition became progressively worse. The picture assumed that of cardionephritis with generalized œdema, convulsions, vomiting, anuria, an irrational state, and beginning choked discs. Heroic measures were apparently used to preserve life. Blood urea and renal functional tests were normal. There was slight improvement and then a more typical tetanic spasm developed.

May 11, the blood calcium was 5.9 mg. for each 100 c.c. This test, together with the clinical signs and symptoms, indicated an atypical case of tetany, and calcium lactate was given in large doses by mouth; the convulsions continued and calcium lactate was

given intravenously with only slight relief. Parathormone was given subcutaneously and still the convulsions persisted. Relief was not obtained until parathormone was given intravenously. The blood calcium was 7.4 mg. for each 100 c.c. On May 25, the blood calcium was 8.56 mg. and there was steady improvement. June 1, the patient was taking 500 grains of calcium lactate and 150 grains of calcium carbonate daily, and 1 grain thyroid extract three times daily. July 12, the blood calcium was 10.1 mg. for each 100 c.c. and the mental condition was more nearly normal. The patient weighed 203 pounds and was walking better. September 20, the blood calcium was 10.25 mg. for each 100 c.c. The patient was feeling well, was more active, and weighed 189 pounds. December 28, the blood calcium was 11 mg. Her condition seemed normal, and she weighed 176 pounds.

Comment.—The unusual features of this case are that symptoms of tetany did not develop until eight months after operation; the atypical onset suggested myxœdema rather than tetany. Repeated basal metabolic tests were normal, however, and no clinical improvement resulted from the administration of thyroxin. The mental evolvement was unusual in my experience. During the entire time the patient maintained a humorous child-like attitude. It was the only case in which blood calcium was not raised by the intravenous injection of calcium lactate. Even the subcutaneous injection of parathormone was ineffective.

Case IV.—A man, aged fifty-six, came to the Clinic March 4, 1926, because of exophthalmic goitre with secondary chronic myocarditis and cardiac arrhythmia. Several months previously his condition had been diagnosed elsewhere as a primary cardiac lesion and he had been confined to bed most of the time since then. He came to the Clinic on the verge of a crisis in an emaciated condition, having lost more than 40 pounds. The basal metabolic rate was + 59. March 18, after eight days' preparation, primary thyroidectomy was performed in the usual manner. The gland was unusually large and showed considerable reversion to colloid; a part of the gland, about one-fourth of a normal-sized one, was preserved on each side.

March 21, the patient complained of a dull pain in the left shoulder, and of numbness and a stinging sensation in the right arm and hand. The right thumb was stiff and immovable. Three days later there were no further complaints and he left the hospital. March 26, the patient complained of numbness and tingling in the hands and feet with a tendency to cramps. Examination showed a bilateral Chvostek's sign 2+. Trousseau's sign was not demonstrable. Beginning tetany was evident. The blood calcium was 6.99 mg. for each 100 c.c., and 100 grains of calcium lactate was given orally three times daily. April 2, the basal metabolic rate was + 20. The patient gained rapidly and there were no further signs of tetany. April 26, he had gained 20 pounds and was much stronger, although he was dizzy at times. He had not been taking calcium lactate for four days but felt slight numbness in the hands and feet. May 5, there were no signs or symptoms of tetany. June 26, the patient had gained 40 pounds, was again taking calcium, but noticed slight numbness in the hands. There was no Chvostek's sign. February 10, 1927, he still had occasional mild cramps in the hands and feet, and Chvostek's sign 1+. Fifty grains of calcium lactate and 10 grains calcium carbonate were given three times daily. February 15, the blood calcium was 8.08 mg.; the patient had been eight days without calcium lactate. He complained of numbness in the hands, and treatment was resumed.

Comment.—In time this condition may clear up and the tetany disappear. The patient had been allowed a general diet because of the mildness of his symptoms. Before his admission he had been bedridden for months and his

condition considered hopeless. He has not regained his health, although he has gained more than 40 pounds. The cardiac arrhythmia has cleared up. He was advised to rest but spent most of the winter hauling logs.

CASE V.—A woman, aged forty-nine, came to the Clinic, May 28, 1925, because of multiple toxic adenoma with secondary hypertension and myocarditis. Her case has proved one of consistently severe and chronic tetany. The marked improvement following exposure to ultra-violet light has been encouraging (Fig. 2).

Thyroidectomy was performed July 9. On the following day the patient complained of stiffness in the hands and feet. July 11, the symptoms persisted and three 30-grain

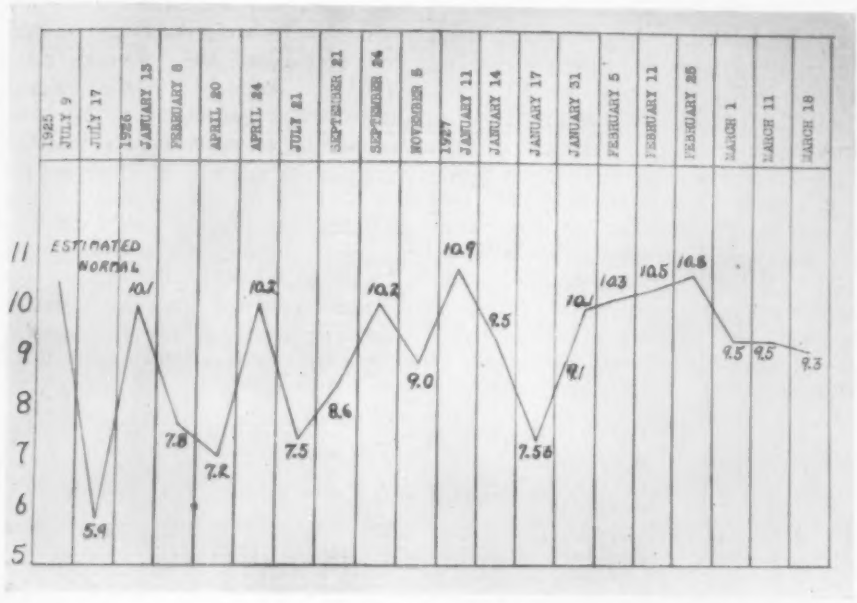

FIG. 2.—The curve shows the effect of the ultra-violet light treatments on the blood calcium in milligrams for each 100 c.c.

doses of calcium lactate were administered during the day. July 15, she left the hospital and July 17, she was re-admitted because of symptoms of severe tetany. She was given 50 c.c. of a 1 per cent. solution of calcium lactate intravenously and July 23, she was taking 120 grains calcium lactate daily. The tetany was controlled. December 2, the hands still showed tetanic contractions and on December 5, she was given two intravenous doses of calcium lactate which considerably improved the condition. They recurred, however, January 6, 1926, and on January 13, Chvostek's sign was 2+. Two intravenous doses of calcium lactate were given in forty-eight hours. January 22 and 23, 1 c.c. of parathormone was given three times daily with immediate relief. February 3, the patient had been taking 100 grains calcium lactate three times daily and began taking 1 c.c. parathormone daily. This relieved the spasm in five minutes. Three days later the condition was much better and she was taking only parathormone. February 8, slight stiffness was noted; the calcium lactate was resumed in 200 grain doses three times daily, and she was dismissed from observation.

April 20, the patient returned with symptoms of severe tetany. Her condition had been good until she stopped taking calcium lactate. She was given a hot bath, and calcium lactate was given intravenously. April 24, she was again dismissed from observation with instructions to take 200 grains calcium lactate three times daily.

July 21, the patient reported that she was feeling well. However, she was not

absorbing the calcium lactate so 25 grains calcium carbonate was added three times daily. September 21, she was feeling well and there were no further symptoms of tetany. She was given 1 c.c. parathormone daily. September 24, the parathormone raised the blood calcium. November 5, she was still feeling well; the calcium lactate was discontinued and the recurrence of symptoms was observed; 1 c.c. of parathormone had no effect but the dose repeated in ten minutes gave relief. January 11, 1927, there were no symptoms of tetany or Chvostek's sign, and all calcium was discontinued for three days. January 12, there was Chvostek's sign 1+ but no Trousseau's sign. January 13, there was Chvostek's sign 2+. January 14, tetany had begun to develop and the patient had to take calcium lactate one hour before the test. She complained of headache and pain in the legs and arms. Erb's sign was +++. On the following day ultra-violet light treatments were begun and 100 grains calcium lactate given three times daily. The regular dosage of calcium lactate was reduced one-half and 10 grains calcium carbonate added three times daily. January 17, tetany developed in the hands and Chvostek's sign was 2+. January 21, the patient's condition was improved. There were no symptoms of tetany. The effect of the ultra-violet light treatments was remarkable, and they were discontinued February 5. February 11, she felt well and returned home for two weeks with the instructions to take one-half the usual dose of calcium lactate. February 25, she reported that she was feeling better than ever; the ultra-violet light treatments were resumed. February 28, the calcium lactate dosage was reduced to 150 grains daily. March 1, there were no signs of tetany. March 11, the calcium lactate was reduced to 75 grains daily. March 18, she was again sent home for two weeks. She complained of occasional slight stiffness in the fingers. August 1, the blood calcium was still normal and the patient was still taking 75 grains calcium lactate a day without further ultra-violet light treatment.

Comment.—This case is the only one in which anything unusual occurred during the course of operation. One-third of a normal lobe was preserved on each side. The gland was friable and the right inferior thyroid artery tore loose. The nerve may have been caught when the artery was sutured as hoarseness followed immediately; consequently the suture was later cut and the vessel tied separately. There was only transitory involvement of the nerve, but possibly the blood supply of the right parathyroid glands was cut off.

CONCLUSIONS

1. The radical type of thyroidectomy necessary to obtain cure and prevent recurrence has resulted in an increased incidence of post-operative tetany.

2. The number of cases of chronic post-operative tetany in the literature is small, possibly because unsatisfactory results are not reported.

3. This series of cases is reported in the hope that it will further stimulate a study of the problem and possibly lead to more satisfactory methods of treatment.

4. Considerable scientific study has been made of this problem, but there is a lack of clinical correlation.

5. Calcium and parathormone are the two agents that have proved most effective in the treatment of tetany. Neither is a cure for the chronic type of tetany.

6. Transplantation of parathyroid glands has not proved generally effective because of the difficulty of recognizing the gland at operation.

7. In this series of cases one patient was markedly benefited by the use of ultra-violet light. Sufficient time has not elapsed to determine the ultimate result.

8. The onset of symptoms may be acute or tetany may develop several months after operation. It may be atypical.

9. Parathormone was used with beneficial but not curative effect in three cases.

10. A diet high in calcium, the prevention of constipation, and plenty of sunshine are advised.

11. As might be expected, tetany has no effect on the basal metabolism. The basal metabolic rate was normal in these cases during the course of the tetany.

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THE USE OF LUGOL'S SOLUTION IN EXOPHTHALMIC GOITRE

AN EXPLANATION FOR THE BENEFICIAL RESULTS OF PRE-OPERATIVE MEDICATION

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That the administration of iodine prior to operation for exophthalmic goitre controls the symptoms, lowers the basal metabolic rate and lessens the hazards of operation, is no longer questioned. This teaching, however, is directly contrary to that of only a few years ago. Formerly the surgical school led by Kocher opposed the use of iodine in any form of Graves' disease, holding that it increases the severity of the symptoms and may, in fact, be responsible for the development of exophthalmic from simple goitre.

The older literature contains numerous reports of unfavorable results from the use of iodine in various states of toxic goitre. We now realize that many of these accidents probably resulted either from the use of excessive doses or from moderate doses too long continued; others followed the administration of desiccated thyroid extract or thyroxin. However, these unfavorable reports served to crystallize in the medical mind a dread of the evil consequences of iodine medication in exophthalmic goitre.

Nevertheless there were occasional reports of remarkable results from iodine therapy. Cheadle,[1] in 1869, reported two cases of Graves' disease showing immediate and extraordinary improvement after iodine treatment. In 1875, he added a second series of six cases. One of the latter was very instructive: The patient improved rapidly during the first two weeks of iodine treatment but then relapsed. This case exemplifies the status of iodine treatment as we see it so commonly to-day.

Marine and Lenhart,[2] in 1911, showed that iodine may produce involution in the hyperplastic thyroid gland and recommended its use to prevent hyperplasia.

Ohlemann,[3] in 1913, reported that he had cured himself of Graves' disease by taking about 150 c.c. of tincture of iodine and a little potassium iodide occasionally over a period of three years.

Neisser,[4] in 1920, disagreeing with the generally accepted view regarding the contra-indication of iodine in exophthalmic goitre, observed notable improvement and freedom from ill effects following the use of small doses.

Loewy and Zondek,[5] in 1921, observed a reduction in the basal metabolic rate and improvement in the nutrition and general subjective condition of the patient after administering a few mg. of potassium iodide daily.

Lugol's Solution for Pre-operative Treatment.——In March, 1922, Plummer [6] began the use of Lugol's solution in the Mayo Clinic as a pre-operative measure for the treatment of exophthalmic goitre. This treatment, as finally elaborated, consists of the administration of 10 minims of Lugol's solution three times a day for the first ten days. This dosage is continued up to operation and throughout the post-operative reaction, even though operation be postponed for several weeks. After the post-operative reaction, 10 minims daily are given as a routine for eight weeks. When a crisis occurs or immediate control is necessary, Plummer advises the administration of from 50 to 100 minims in divided doses by mouth or rectum within one or two hours.

Plummer [7] reports that the pre-operative use of Lugol's solution in the Mayo Clinic

reduced the surgical mortality from 3.5 per cent. to approximately 1 per cent. Likewise, the pre-operative mortality was decreased from 2.5–3 per cent. to 0.2–0.5 per cent., and the fatalities in the treated group occurred from complications not attributable to the condition of the thyroid gland.

Plummer and Boothby,[8] in 1924, reported on the use of Lugol's solution as a pre-operative measure in cases of exophthalmic goitre. In a series of 600 cases, no patient with unquestioned exophthalmic goitre was made worse by the treatment; approximately two-thirds were greatly benefited; only one patient in twenty was not demonstrably improved. The Lugol's solution was given in an average dose of 10 drops daily, well diluted and followed by a glass of water. When not tolerated by mouth, it was administered by rectum. The latter route, however, was required only for patients with severe gastro-intestinal crises and then only for a few days.

The observations of Plummer and Boothby have been abundantly confirmed. Mason,[9] in 1924, showed that compound iodine solution controls the toxicity arising from regeneration of thyroid tissue after thyroidectomy. This result he interpreted as an indication that the increased activity of the regenerated cells is of the same, or closely allied, nature as that of the cells of the original gland.

Starr and Means [10] in the same year reported excellent results following the administration of 15 drops of Lugol's solution daily to patients with exophthalmic goitre. In some cases the basal metabolic rate fell within a few days from plus 50 or 60 to plus 10 or 20; in others, to normal or even below. The pulse became slow and the appetite normal, nervousness and tremor diminished, and the weight increased. They concluded that the use of Lugol's solution by mouth produces abrupt remissions in many cases of exophthalmic goitre. In a later communication, Starr, Walcott, Segall and Means [11] showed that the remission after iodine treatment is as immediate and extensive as that following subtotal thyroidectomy, but that iodine alone cannot suppress Graves' disease permanently. If iodine medication is discontinued, a rapid rise of the basal metabolic rate and an exaggeration of the symptoms occur within one or two weeks. Like Plummer and Boothby, they observed that iodine medication is sometimes without effect.

In 1925, Boothby [12] reiterated that iodine, given to patients with exophthalmic goitre, usually reduces the basal metabolic rate and practically always causes the nervous and gastro-intestinal symptoms to disappear. However, he cautioned against its use in cases of adenomatous goitre without hyperthyroidism, since toxic symptoms may be induced thereby. Properly administered, Lugol's solution, according to Boothby, prevents death from acute post-operative exophthalmic goitre crisis. He believes that, with a few exceptions, iodine should be given only as a temporary therapeutic measure to bring the patient into a safe condition for partial thyroidectomy.

Read,[13] in 1925, reported twenty-six cases of thyrotoxicosis, in some of which operation had been performed, in which compound iodine solution was administered. In eleven cases there was marked improvement; in eight, moderate benefit; in six, slight or negligible change. No patient in the series was made worse by the treatment.

Clute,[14] in 1926, reported on the use of iodine as a pre-operative measure in association with rest in bed for from seven to ten days. Sixty-nine cases were selected for detailed study. It was found that before the use of Lugol's solution and rest in bed, only 38 per cent. of patients were operated on in one stage; whereas, since the installation of that treatment, 63.7 per cent. were operated on in one stage.

In Switzerland, Merkle [15] confirmed the excellent results of using Lugol's solution as a pre-operative measure in cases of exophthalmic goitre. In his experience, the optimum condition was obtained after eight days of treatment; but this improvement was only temporary, and the condition became worse when treatment was discontinued. He therefore believes that iodine should be used only as a preparation for operation.

Helmholz,[16] in 1926, reported on the use of Lugol's solution as a pre-operative

measure for exophthalmic goitre in children. In thirty cases occurring in children under the age of fifteen, compound iodine solution, administered in doses of from 5 to 10 minims three times a day, reduced the basal metabolic rate and controlled the toxic symptoms to a marked degree. In fourteen of the cases, the average reduction following iodine medication was 19 points. In the last eleven cases, the treatment made preliminary operation unnecessary.

Graham [17] believes that the pre-operative administration of Lugol's solution is safe and beneficial not only in exophthalmic goitre, but also in so-called toxic adenoma. In his opinion, the condition of the thyroid gland itself determines the one and only indication for the administration of iodine to any patient with goitre. If the gland is hypertrophic and hyperplastic, preliminary iodine is indicated, regardless of clinical grouping and the presence or absence of adenoma. On the other hand, if the thyroid is in a colloid or resting state (involution, not degeneration), there is no indication for iodine so far as thyroid function is concerned, and its use may be detrimental.

Altogether the great mass of clinical evidence substantiates the view that the pre-operative administration of compound iodine solution in cases of exophthalmic goitre is a safe and decidedly beneficial measure.

How Lugol's Solution Acts.—With regard to the manner in which Lugol's solution acts, there is great diversity of opinion. Plummer [18] attributed the toxic symptoms of Graves' disease to iodine starvation, resulting in incomplete iodization of the hormone thyroxin. His theory was that, without the addition of sufficient iodine, the thyroxin is toxic; that is, that the iodine in the gland detoxicates the thyroxin. This hypothesis, however, is not supported by sufficient facts.

For some time past in connection with my operative work on patients with hyperplastic goitres, I have repeatedly made an observation which, I believe, throws some light on the mechanism by which Lugol's solution acts. When the patient has been treated with a preliminary course of compound iodine solution, the thyroid gland at operation is found to be very œdematous. When the gland is sectioned, a watery fluid exudes freely from the cut surfaces. This condition is not true of hyperplastic thyroids not treated previously with Lugol's solution, nor of ordinary colloid goitre.

This observation has led me to believe that the beneficial effects of iodine medication are brought about by a rapid formation of colloid material in a gland famished for iodine, resulting in back pressure not only on the cells and acini, but also on the thin-walled veins surrounding the acini. In my opinion, this back pressure causes the passive œdema that we find at operation.

It is reasonable to suppose that the œdematous condition of the gland renders the secreting cells temporarily inactive, thus effectively preventing the absorption of the toxic substance. Hence the patient's condition improves. In the course of time, however, new blood-vessels are formed and the older ones gradually accommodate themselves to the changed condition. Then absorption takes place again and the patient once more becomes toxic, even though the colloid formation may still persist in the gland.

A similar conclusion to mine has been reached by Marine,[19] who studied the effects of iodine administration in various lower animals. Marine observed that in dogs the thyroid gland, previously soft and spongy because of the marked hyperplasia, became very firm as early as the fourth day after the administration of large doses of tincture of iodine. Numerous histologic examinations showed this firmness to be due to the accumulation of colloid material. Marine also calls attention to a clinical fact observed in connection with the iodine treatment of simple goitre. Such patients often return about seven days after beginning treatment, complaining that the gland is actually larger, firmer to the touch and very painful (so-called iodine thyroiditis).

My clinical observations on the condition of hyperplastic thyroid glands found at operation in patients previously treated with Lugol's solution have led me independently to reach the same conclusion as Marine,[20] who formulated his views as follows:

"A much more rational view of the beneficial effects of iodine in cases of Graves' disease with marked hyperplasia is that the administration of large doses of iodine (especially inorganic) causes a rapid accumulation of colloid in the alveolar spaces just as the administration of iodine to cases with marked hyperplasia of other clinical associations in man, dogs, sheep, birds and fish. The rapid distention of the alveoli with colloid brings about a *pressure retention* which temporarily blocks excretion until the thyroid cells have accommodated themselves to the increased tension. Excretion is then reëstablished and the metabolism begins to rise."

Other workers have reported observations on changes in the structure of hyperplastic thyroid glands as a result of iodine medication. Cattell[21] showed that iodine therapy causes marked changes both in the iodine content of the gland and its pathologic structure. He found a direct ratio between the degree of involution and the iodine content, thus confirming the observation that the iodine content of the hyperplastic thyroid gland is inversely proportional to the degree of hyperplasia. Pathologically, he found the papillary projections with high epithelium replaced by vesicles lined with low epithelium and filled with colloid material.

In a comparative series of thirty patients with Graves' disease, fifteen of whom were treated pre-operatively with iodine and fifteen without, Rienhoff[22] established the fact that preliminary iodine therapy is associated with a change in the histologic appearance of the gland from a hyperplastic to a colloid state, even though there is definite evidence of the hyperplasia still remaining. He observed that after iodine treatment the size of the gland as a whole is increased but that its vascularity, and probably also the lymph flow through the gland, is diminished. There was a striking increase in the amount of colloid deposited within the gland and also a large increase in the amount of fibrous connective tissue. Definite changes were observed in the acini. They were transformed from lace-like papillomatous ingrowths to round, even-walled, smooth acini of regular size and form. High columnar epithelium gave way to flat cuboidal and occasionally low columnar epithelium. The large clear nuclei of the epithelial cells in the untreated glands were replaced by the small, irregular, pycnotic type in the treated glands. Mitotic figures in the nuclei, so common in untreated cases, were absent when the patient received preliminary iodine medication. Rienhoff likens the change produced by iodine medication to an artificial remission of the thyroid hyperplasia.

Giordano[23] likewise found histologic evidence supporting the view that involution changes occur in the thyroid gland when iodine is administered to patients with exoph-

thalmic goitre. In general, the degree of this involution closely paralleled the clinical course. The changes resembled those following preliminary ligation of the thyroid vessels, except that they were distributed uniformly throughout the gland.

SUMMARY

It is now fully established that the pre-operative administration of Lugol's solution to patients with exophthalmic goitre lowers the basal metabolic rate, controls the toxic symptoms and lessens the hazards of operation. However, opinions as to the mechanism by which iodine medication benefits the patient are still far from unanimous.

That the toxic symptoms of Graves' disease are associated with iodine starvation of the thyroid acini, cannot be questioned. Hence it was reasonable to assume that iodine acts by detoxicating an incompletely iodized thyroxin molecule. This view, however, is largely speculative and not supported by sufficient evidence.

In removing hyperplastic thyroid glands of patients previously subjected to iodine medication, I have repeatedly observed that the glands are very œdematous; so much so, that water exudes freely from the cut surfaces when the glands are sectioned. This condition is not true of hyperplastic glands without iodine treatment, nor of ordinary colloid goitre.

From this observation I have come to believe that the beneficial influence of Lugol's solution is brought about by a rapid formation of colloid material in the iodine-famished gland, resulting in back pressure on the secreting cells and the thin-walled veins surrounding the acini. Hence passive œdema follows and the cells, rendered temporarily inactive, fail to absorb the toxic substance; consequently the patient's clinical condition improves. In the course of time, new blood-vessels are formed and the older ones accommodate themselves to the changed conditions, so that absorption is resumed and the patient again becomes toxic, notwithstanding the fact that the colloid material may persist in the acini.

The explanation I have given would account for the fact that improvement from iodine medication is only temporary. It is in accord with Marine's views, based largely on experimental observations on animals, and consistent with the recorded changes in thyroid glands removed after preliminary treatment with Lugol's solution.

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EFFECT OF HYPERTHYROIDISM UPON DIABETES MELLITUS

STRIKING IMPROVEMENT IN DIABETES MELLITUS FROM THYROIDECTOMY

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We wish to emphasize the remarkable improvement in carbohydrate tolerance following subtotal thyroidectomy in diabetes mellitus complicated by hyperthyroidism, and to discuss important factors in the management of this problem, more particularly from a surgical viewpoint. This specific syndrome has in the past been attended with a high mortality which has now been almost eliminated since both conditions can be improved to a point where operative removal of portions of the thyroid can be done without undue risk.

Diabetes mellitus is a condition in which less than the normal amount of glucose can be oxidized in a unit of time. When the fat burned is more than four times the glucose burned acidosis occurs. If the diet does not supply the total calories, the extra calories of the metabolism are derived from body fat. In hyperthyroidism with its high metabolic rate, the total metabolism may be twice that of the ordinary diabetic patient, accordingly, when these two conditions exist together the usual diabetic diet may supply half or less of the calories consumed and the remainder will come from the patient's body fat. The entrance of this very large amount of fat into the metabolic mixture, combined with the inability to oxidize a sufficient amount of glucose (because of the diabetic state), results in acidosis. The use of insulin in amounts sufficient to cause the combustion of the proper amount of glucose on one hand, and the lowering of the metabolic rate by iodine on the other hand, work together to bring the patient to a safe condition for operation.

The literature bearing upon the subject has been reviewed recently from a clinical metabolic standpoint by Wilder [1] and from an experimental viewpoint by Allen.[2] The surgical aspects of this problem have not been comprehensively dealt with, although occasional case reports have appeared. The surgical attack on the thyroid has been carried out on (a) normal glands, (b) adenoma with and without hyperthyroidism and (c) exophthalmic goitre.

O'Day,[3] encouraged by the improvement in sugar tolerance by thyroidectomy in four diabetic patients with exophthalmic goitre, operated upon the thyroid of two young patients with diabetes but with "no goitre symptoms" and reported restoration of normal carbohydrate tolerance in one, and nine ounces of carbohydrate a day in the other. Crile,[4] in a fascinating article on the "kinetic drive," described a series of operations on a patient with severe diabetes consisting of section of both cervical sympathetic

trunks, left suprarenalectomy and partial thyroidectomy with some improvement in sugar tolerance of a patient without evident thyroid disease. Fitz[5] was not particularly encouraged by the results of operation in this group of cases, although his observation led him to believe that "occasionally an operation may not only prolong life but be of greater benefit." He describes five patients with non-toxic goitre on whom thyroidectomy was done without mortality or benefit to the diabetes; six patients with exophthalmic goitre with one operative death, and six with adenomatous goitre with hyperthyroidism with one death. The diabetes was greatly benefited in one case of exophthalmic goitre and in three cases of adenomatous goitre. The results reported by Fitz and our own which confirm his findings in cases of diabetes mellitus and adenomatous goitre without hyperthyroidism as well as the experimental work of Allen lead us to the conclusion that the removal of a normal thyroid or a goitre without hyperthyroidism will not benefit the associated diabetes mellitus. Wilder[4] analyzes 15 cases of exophthalmic goitre and 23 cases of adenomatous goitre with hyperthyroidism associated with diabetes mellitus. Thirty-three of these cases were operated upon without a death and he concludes that thyroidectomy is almost always followed by a considerable gain in sugar tolerance. He finds that diabetes mellitus complicating hyperthyroidism does not exceed 1.1 per cent. being more frequent in the adenomatous group, 2 per cent., than in the exophthalmic group 0.6 per cent.

Rohdenburg[6] reports thyroidectomy in two cases of exophthalmic goitre with diabetes with improvement in the latter condition.

Dyas[7] reports three cases of exophthalmic goitre with glycosuria and probable diabetes treated by thyroidectomy without death. All cases remained sugar free following operation on unrestricted diet during a period of observation of several weeks. Unfortunately no blood sugar studies are given.

Buchanan[8] reports a case of diabetes mellitus complicated by hyperthyroidism with thyroidectomy and great improvement in carbohydrate tolerance.

Hubbell[9] briefly mentions a case operated upon with improvement in diabetes.

Falta[10] reports irradiation of the thyroid in six cases of exophthalmic goitre with diabetes and apparent improvement in the carbohydrate tolerance in four of them.

Glycosuria of a mild and transient nature occurring with hyperthyroidism has been described frequently in the literature and was encountered often in our experience. Fasting hyperglycæmia is a rare occurrence, although a high normal value is frequently seen. Alimentary hyperglycæmia following a test meal is frequent. There is no close relationship between the severity of the hyperthyroidism as determined by the basal metabolic rate and the hyperglycæmia. The curve obtained following sugar ingestion is that of the emotional type. In the University Hospital is a large diabetic clinic and all cases with hyperglycæmia are carefully studied there. The cases described in this report were referred to us from this group as cases of diabetes mellitus.

Since June, 1924, there have been 1150 cases of diabetes mellitus treated in this clinic. Of this number 12 cases were complicated by hyperthyroidism. All were treated by operation with one death. Eleven of these cases were adenomatous goitre with hyperthyroidism and one was a case of exophthalmic goitre. Many facts can be demonstrated by the report of a typical case:

CASE I.—(No. 160,668) *admitted in diabetic coma: insulin with prompt improvement, continuation of medical treatment for several weeks. Subtotal thyroidectomy. Apparent cure of diabetes.*

Mrs. S., housewife, age thirty-one, had increased thirst and polyuria for two months

with loss of 15 pounds in weight associated with a moderate degree of nervousness and palpitation. One week before entrance she felt drowsy, became irrational and was brought to the hospital for treatment. Examination showed confused mental state, Kussmaul hyperpnœa, sweating, a small goitre and tachycardia. She was considered to be in extremis. The urine contained large quantities of sugar and the acetone bodies. The plasma CO_2 combining power was 24 volume per cent. The blood sugar 267 mgm. per 100 c.c. She was treated with the usual anti-coma methods with considerable improvement for several days. It was then more clearly seen that there was a definite nervousness, tachycardia and sweating and hyperkinesis. A basal metabolic rate was

CHART I

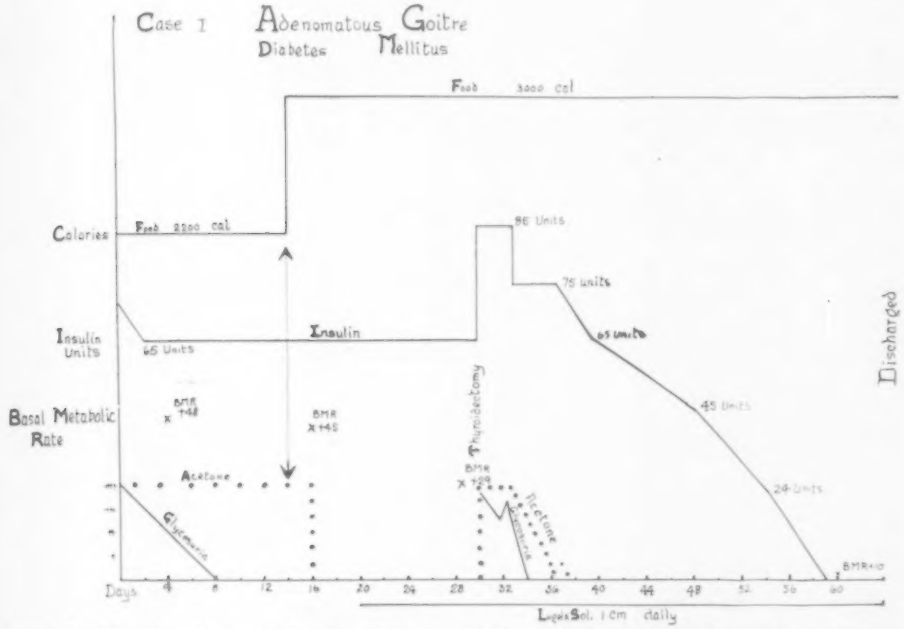

CHART I.—This chart illustrates the effect of diet on acidosis; and of operation on carbohydrate tolerance, basal metabolism, insulin requirements, and acidosis.

45 per cent. plus. She was treated with a diet of protein 55, fat 170, carbohydrates 45, supplying 2200 calories and 65 units of insulin were required daily. She immediately became sugar free except for a faint trace. Diacetic acid remained in the urine in large amounts. The diet was changed to protein 60, fat 275, carbohydrate 75, supplying 3000 calories and the urine became acetone free. After seventeen days of study and treatment she was given compound solution of iodine, one c.c. daily for nine days with a resulting drop in the basal metabolic rate to 29 plus. Subtotal thyroidectomy was done and followed by an uneventful convalescence except for a glycosuria and acetonuria for four days. The insulin dosage was gradually reduced so that on the twenty-third post-operative day she remained sugar free for the first time without insulin on a diet of 3000 calories. She was discharged on this diet and has gained steadily in weight and strength. She has an occasional transient glycosuria. The glucose tolerance curve, typical of diabetes mellitus before operation did not vary essentially following it.

This case illustrates well the possibility of the restoration to an approximately normal condition of a moribund patient with diabetes mellitus. The progress of the case is shown graphically in Chart I. The chief factor, leading to permanent improvement by operation, after the abolition of the acute

acidosis was the recognition of the presence of hyperthyroidism. This was not at once apparent since the goitre was very small and the symptoms of tachycardia and nervousness were attributed to the acidosis. Its recognition also gave an important aid in the dietary treatment, as it can be seen in Chart I that a high grade of acetonuria persisted for days after glycosuria had ceased. It could be predicted after the determination of the metabolic rate that the acidosis would disappear by raising the total number of calories, since the original diet was based on a normal metabolic rate and neglected

TABLE I.

Demonstrating the Great Improvement in Hyperthyroidism and Carbohydrate Tolerance Effected by Thyroidectomy.

Case No.	Admission weight	Weight loss in pounds	Time in months	Initial basal metaboliam	Pre-operative basal metabolism	Post-operative basal metabolism	Days of iodine	Pre-operative insulin daily in units	Pre-operative diet in calories	Post-operative insulin discontinued	Post-operative diet
1	136	35	8	55	40	16	8	None	2400	3 days	2400
2	125	45	?	49	33	3	12	U.13	2400	25 days	2400
3	115	40	?	54	36	2	21	U.45	2400	18 days	3010
4	114	15	2	48	29	10	9	U.65	3000	22 days	3000
5	113	34	6	49	25	13	20	U.36	2500	7 mos.	2500
6	100	55	11	29	29	6	—	None	House Diet	16 days	2400
7	90	42	3	75	57	–	41	U.90	3000	—	
8	105	64	18	33	8	2	—	None	2330	5 days	2400
9	108	57	10	22	14	2	—	None	2400	7 days	2400
10	125	20	5	72	57	12	13	U.40	3000	15 days	2400
11	106	30	6	45	38	4	19	U.108	3000	29 days	
12	90	17	3	63	33	7	22	U.50	3000	16 days	2400

the 50 per cent. increase in the basal rate that was present. She was living on her body tissues and the calories provided by her fats were insufficiently covered by glucose to be completely burned. As soon as her quantitative caloric requirement was met, the acidosis disappeared. It is especially noteworthy that in the adequate diet the high fat ratio of the diet was maintained. Thus in the diabetic patient an increase of the general metabolism must be met by an adequate diet for the caloric requirements of the body.

Following thyroidectomy there occurs an immediate but brief increase in the metabolism. With all cases there was a mild or moderate glycosuria and acidosis lasting from four to seven days following operation. This indicates the need for more calories in the form of glucose and an increase

in the amount of insulin at this time. After operation, when the basal metabolic rate has dropped to normal, there is a marked increase in the carbohydrate tolerance. In all cases in the series, insulin, if needed before operation could eventually be dispensed with even with a high caloric diet. This was possible within one month after operation with the exception of Case V, in which the insulin though much reduced could not be entirely dispensed with for seven months. This patient was pregnant in addition to having diabetes mellitus and hyperthyroidism. This improvement in function is well shown in Table I. It must be emphasized that the diabetic state is not cured by thyroidectomy but is improved to such an extent as to simulate a cure. The glucose tolerance tests following the post-operative improvement of function in our series were of the diabetic type. In many of the cases careful dieting had to be followed after operation for an indefinite period.

It will be seen from Table I that two patients were in coma at the time of entrance to the hospital. These cases offer no unusual difficulties either in diagnosis or treatment. Of greater interest to the surgeon is the onset of diabetic coma following thyroidectomy in a supposedly non-diabetic patient. As already stated the entire carbohydrate metabolism is upset by hyperthyroidism and especially by the severe but transitory exacerbation following operation, so that a mild or unrecognized diabetic may have a dangerous and stormy post-operative course. This is illustrated by Case II.

Case II.—(No. 124,843.) *Adenomatous goitre; mild glycosuria on one occasion before operation. Subtotal thyroidectomy followed by diabetic coma on second post-operative day. Medical treatment. Cure.*

Mrs. B., a housewife of fifty-eight, entered the surgical ward for treatment of goitre and nervousness of three years' standing. She was overiodized before entrance by use of a patent medicine with accentuation of all symptoms during the previous four months. Loss of fifty-eight pounds in ten months. Increased thirst for one year. Examination showed an emaciated elderly woman with an adenomatous goitre of moderate size, arteriosclerosis, pulmonary emphysema, cardiac enlargement and compensated myocardial disease. Basal metabolic rate plus 29 per cent. She was treated with bed rest and a high caloric diet for two weeks. On one occasion there was a moderate glycosuria but on three other examinations the urine was sugar free. The glycosuria was regarded as of the transitory type seen in simple hyperthyroidism and the carbohydrate metabolism was not studied. Subtotal thyroidectomy was done unaware of the presence of diabetes. On the day following the operation she became comatose, developed deep respirations, an acetone breath and a severe glycosuria, acetonuria and hyperglycæmia were demonstrated. She was treated with large doses of insulin and glucose given intravenous with restoration to a satisfactory state. After this 45 units daily of insulin were required for one week. On the eighteenth post-operative day insulin was discontinued and she tolerated a house diet of 2500 calories without glycosuria.

This case demonstrated the need for a careful investigation of the carbohydrate metabolism in all patients with hyperthyroidism and glycosuria. We believe it important in these cases to make a quantitative determination of the excreted sugar on a known diet and of the blood sugar with the standard glucose tolerance test in these cases.

Another complication which arose in the treatment of one of these cases was the confusion of diabetic acidosis with its exaggerated hyperpnœa, cya-

nosis and mental obfuscation with tracheal obstruction. This is illustrated by Case III.

CASE III.—(No. 16,518.) *Severe diabetes and hyperthyroidism. Diabetic coma on two previous occasions. Difficulties in dietary management. Subtotal thyroidectomy. Diabetic coma resembling tracheal stenosis; tracheotomy, broncho-pneumonia, death.*

Mrs. E., a housewife of forty-four, had noticed thyroid enlargement for eleven years with thyroidism for the past twelve months. Two months before entrance she had polydipsia and polyhagia. Diabetic coma occurred with treatment by local physicians who were later unable to control diabetes. She had lost forty-two pounds in four months. Examination showed an emaciated, very nervous woman with hyperpigmentation of the skin and a large solitary adenoma of the thyroid. Basil metabolic rate plus 90 per cent. Typical diabetic glucose tolerance curve. CO_2 combining power of plasma 30 volumes per cent. Intense glycosuria and acetonuria. She was placed on a diet of 2600 calories with 100 units of insulin daily. There was considerable nausea, vomiting, diarrhœa, epigastric pain with attacks of dyspnœa and precordial distress. The urine could not be kept consistently free of acetone or glucose. She developed bronchopneumonia which added to the difficulties of treatment but which cleared up in twelve days. Eventually she began to gain weight on a diet of 3000 to 5000 calories with large doses of insulin. The compound solution of iodine was given, one c.c. daily for forty days. The basal metabolism then had fallen to plus 57 per cent. and she was less nervous. A subtotal thyroidectomy was done easily and rapidly under ethylene anæsthesia. On the evening of the operation the respirations became labored and she became cyanotic and comatose. An emergency tracheotomy was done by the house surgeon without relief of symptoms. The subsequent administration of glucose and insulin restored the breathing to a normal state. Bronchopneumonia again developed and she died in four days. Autopsy showed a chronic atrophic interstitial pancreatitis; bronchopneumonia; diphtheritic infection of wound; mediastinitis.

This experience, occurring as it did in this series, is recorded with no great feeling of pride to demonstrate the need of wise judgment to prevent confusion between two superficially similar conditions each demanding immediate action. More careful and discriminating clinical observation would undoubtedly disclose the true situation. The important distinction between the two types of respiratory difficulty is the presence of stridor with laryngeal narrowing in the obstructive respiratory condition.

SUMMARY OF CASES *

CASE I.—A Jewish woman of fifty-four, complaining of headaches and hot flashes; symptoms of hyperthyroidism for five months and diabetic symptoms for two months. Examination showed nervousness, an adenoma of the thyroid, and œdema of the ankles. Blood pressure $\frac{170}{88}$. Urine showed a moderate glycosuria and acetonuria on entrance. Secondary polycythæmia. Typical diabetic response to glucose tolerance test before and after operation. Pathological report of thyroid: Multiple adenomas with abundant colloid.

CASE II.—An American woman of forty-six with latent syphilis, hyperthyroid symptoms of one year's duration, had had a moderate diabetes for eighteen months. Coma one week before entrance for forty-eight hours. Blood sugar on entrance 0.200 grams. Diabetic glucose tolerance curve. Diphtheria three weeks after operation. Thyroid pathology: Adenomatous goitre.

CASE III.—An American woman of fifty-five had a large goitre for thirty years with hyperthyroid symptoms of two months' duration. Glycosuria found on routine examina-

* These cases correspond by number with cases in Table I.

tion. Myocarditis with auricular fibrillation. Lenticular opacities. Fasting blood sugar 0.217 grams. Typical diabetic glucose tolerance response. Pathological report: Adenomatous goitre with abundant colloid.

CASE IV.—See text, Case I.

CASE V.—An American woman of thirty-eight had a goitre for seventeen years, diabetes mellitus nine years; hyperthyroid symptoms one year. Hypertension. Two months' pregnancy at the time of operation. Glucose tolerance of the diabetic type. Excreted 26 grams of glucose on 2400 calorie diet without insulin. Pathological report: Multiple adenomas; localized patches of lymphoid hyperplasia. This patient needed insulin until after parturition to cover a high maintenance diet. This was then discontinued. She has gained 26 pounds in one year.

CASE VI.—See text, Case II.

CASE VII.—See text, Case III.

CASE VIII.—A Jewish housewife of fifty-two had a goitre for ten years with diabetic symptoms for eighteen months. Severe glycosuria on entrance with a moderate acetonuria. Auricular fibrillation and chronic myocarditis. Evidence of manic depressive psychosis while in the hospital. Fasting blood sugar 0.160 grams. Typical diabetic glucose tolerance response. Pathological report: Adenomatous colloid goitre.

CASE IX.—A male American paint sprayer of fifty-three had symptoms of diabetes for one year with nervousness. Onset was of rather severe hyperthyroidism five months ago. Neuroretinitis. Intense glycosuria on house diet. Fasting blood sugar 0.166 grams. Typical diabetic glucose tolerance curve both before and after operation. Pathological report: Graves' constitution adenomatous thyroid.

CASE X.—An American housewife of fifty-nine had a goitre for many years; nervousness, tachycardia, fatigue for three months. Examination showed an orange-sized adenoma of the left thyroid lobe, cardiac enlargement, signs of hyperthyroidism with marked tracheal compression. Typical diabetic glucose tolerance response. Intense glycosuria on a house diet. Pathological report: Colloid goitre with large degenerating adenomas. Auricular fibrillation for one week following thyroidectomy but an otherwise uneventful convalescence.

CASE XI.—An American housewife of forty-five complained of headache, loss of weight and slight œdema of the extremities. Mild hyperthyroidism for six months. Examination showed a large adenoma of the thyroid; neuroretinitis with arteriosclerotic changes. Typical diabetic glucose tolerance curve. Intense glycosuria and acetonuria on entrance. Pathological report: Adenomatous goitre.

CASE XII.—An American schoolgirl of sixteen had symptoms of diabetes for three months, with severe symptoms of hyperthyroidism in the same period following a severe emotional upset. Examination showed a chronic bilateral otitis media in addition to the classical picture of Graves' disease. Diabetic glucose tolerance curve. Marked glycosuria on entrance. Pathological examination of thyroid; exophthalmic goitre.

SUMMARY

1. Great improvement of carbohydrate function follows thyroidectomy in the syndrome of hyperthyroidism and diabetes mellitus. This is probably never a "cure" of the latter condition.

2. Thyroidectomy does not benefit carbohydrate tolerance in non-toxic thyroid states.

3. Glycosuria occurring in hyperthyroidism is an indication for study of the carbohydrate metabolism. Coma may result as a post-operative complication of thyroidectomy consequent upon an unrecognized coexistent diabetes mellitus.

4. Care must be taken to rule out diabetic coma in cases of suspected tracheal obstruction.

5. Acidosis frequently results in hyperthyroidism with diabetes due to an insufficient number of calories provided in the diet.

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INTRAPLEURAL PRESSURE IN POST-OPERATIVE ATELECTASIS

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In 1908, Pasteur [1] called attention to massive collapse of the lung as a not infrequent complication of major operative procedures. Since that time numerous articles dealing with the condition have been published. The literature has been extensively reviewed by Scott,[2] Churchill,[3] Jackson and Lee,[4] and others, and for a complete résumé of the subject the reader is referred to their papers. In spite of the excellent clinical studies which point out the diagnostic criteria, the etiology of the condition remains obscure and its experimental reproduction is wanting.

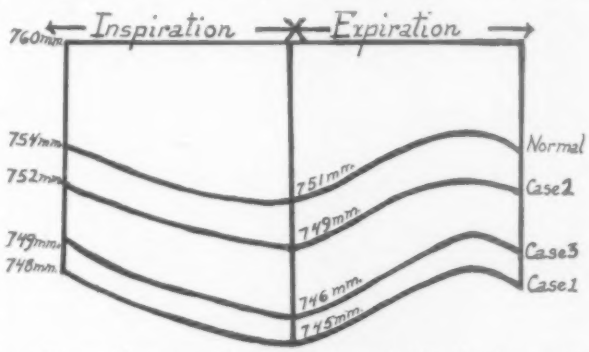

Fig. 1.—Diagram representing the lowered intrapleural pressures in three cases of massive atelectasis, as compared to the normal pressure.

The purpose of this article is to call attention to the value of estimating the intrapleural pressure as a diagnostic aid, and as a means of differentiating post-operative atelectasis from other pulmonary complications. So far as can be determined, no previous estimations of the intrapleural pressure in this condition have been recorded in the literature.

Normally the intrapleural pressure varies from minus 9 mm. of mercury on inspiration to minus 2 mm. of mercury on expiration.[5] Expansion of the alveolar spaces is due to the pull of this negative pressure. Should the pressure become positive, as in pneumothorax, collapse of the lung results with displacement of the mediastinal contents into the contralateral area of lesser pressure. However, in atelectasis, or massive collapse, the mediastinal contents are displaced *toward* the side of the lesion. This displacement is the most characteristic physical sign, and together with the marked narrowing and retraction of the intercostal spaces, indicates a very definite lowering of the intrapleural pressure. Such a lowering is thought to be secondary to the lowering of the intrapulmonic pressure through deflation and collapse of the lung. The exact cause of this deflation is still a matter of conjecture, and may be due to one of several causes. Each of the cases here reported is apparently due to a different cause; the first to bronchial plugging by mucus, the second

to some reflex nervous phenomenon, and the third to bronchial occlusion by a metastatic growth.

CASE REPORTS.—CASE I.—I. J., a negro male, age eighteen, entered the Emory University Division of the Grady Hospital, April 13, 1926.

There was nothing of importance in his history except the story of a right inguinal hernia of three years' duration. Twenty-four hours before admission to the hospital this hernia became caught in the scrotum and the patient was unable to reduce it.

Immediate operation was done under ether anæsthesia. The anæsthetist noted a large amount of bronchial mucus and the necessity of deep anæsthetization to secure relaxation. Incision over the hernial mass disclosed an empty sac, with dense infiltration and œdema of the tissues. The intestines were red and inflamed, but there was no evidence of gangrene. The hernial defect was repaired after the manner of Bassini.

FIG. 2.—Case I. Röntgenogram, three days after operation. The entire right side is clouded, and the displaced trachea with its bifurcation is sharply contrasted. The heart is so displaced to the right that the left border cannot be seen. There is a definite narrowing of the intercostal spaces on the right side.

On the day following the patient's temperature was 104° F., pulse 120, respiration 30. No examination of the chest was recorded.

Forty-eight hours after operation the house officer noted diminished respiratory excursions on the right side with dulness and diminished tactile fremitus. The left chest was normal. Temperature 103° F., pulse 132, respirations 36.

On the third day post-operative it was evident that there was something more than a pneumonia present in the patient's chest. He was inclining toward the right side, and when placed straight in bed would quickly resume that position. There was a definite retraction and narrowing of the right intercostal spaces, and expansion was limited on that side. The right chest was flat to percussion except in the upper part near the sternum where the note was that of high-pitched wooden tympany. In this area the breathing was amphoric, but elsewhere on the right side the breath sounds were absent or distant. Tactile fremitus and whispered voice were absent except over the area of amphoric breathing, where both were increased. The heart was entirely on the right side, with the left border corresponding with the left sternal margin. The right border of the heart and the liver dulness could not be differentiated from the dulness of the lung. A diagnosis of post-operative atelectasis was made and the diagnosis confirmed by röntgenogram (Fig. 2).

During the first week after the operation the condition of the patient remained unchanged, except for the expectoration of large amounts of thick, foul, tenacious sputum.

April 24, eleven days after the operation, the intrapleural pressure was estimated. A needle attached by a rubber tubing to a U-tube manometer containing water was

used.* On introducing the needle into the right pleural cavity the pressure fell to what was equal to minus 12 mm. of mercury and on inspiration the water in the tube rose to an equal of minus 15 mm. of mercury and started over the proximal limb of the tube (Fig. 1). The pressure on the left side ranged from minus 6 to minus 8 mm. of mercury.

The patient continued to expectorate a large amount of thick tenacious sputum, especially when placed on his left side. April 26, fourteen days after operation, there were signs of beginning aëration and a return of the heart to its normal position.

By April 30 his temperature, pulse and respirations were normal, and he was discharged from the hospital on May 21, thirty-one days following operation. His

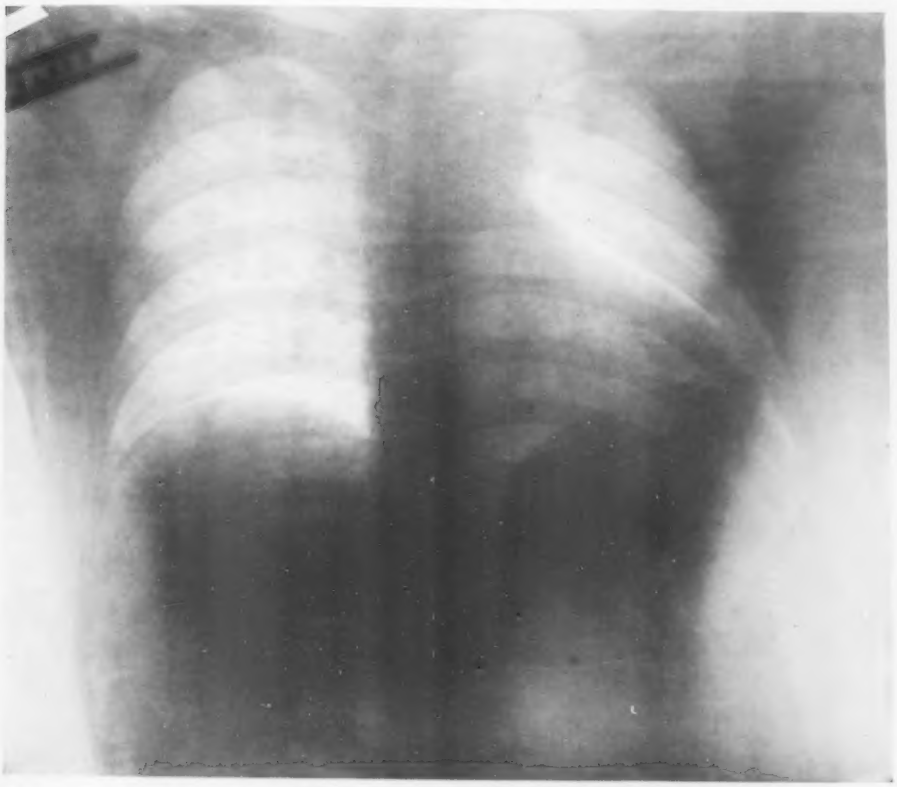

FIG. 3.—Case II. Röntgenogram, four days after dislocation of shoulder. There is displacement of the mediastinal structures to the left, with narrowing of the intercostal spaces.

wound healed without infection and three months later examination showed his chest to be normal in every respect.

CASE II.—A. R., a white section foreman of forty-four, entered Wesley Memorial Hospital, October 18, 1926. Three days before, as a result of a railroad accident, he suffered a fracture-dislocation of the left humeral head and a fracture of the left tibia. There was no evidence of trauma to the chest other than a superficial bruise in the axilla. There was no respiratory difficulty, no cough, and no cyanosis, but the left

* In cases of increased positive pressure due to pneumothorax it has been shown by Graham[4] that the pressure in the contralateral side is increased. For that reason an estimation of the pressure was made on both sides in the three cases here reported. The readings have been translated into terms of mercury since estimations are usually recorded in that manner.

side of the thorax was markedly retracted, and the intercostal spaces were hollowed and narrowed. The apex of the heart was in the left anterior axillary line, and the trachea was displaced toward the left. The lung showed impaired resonance on percussion, and the breath sounds were weak and distant (Fig. 3).

The intrapleural pressure was estimated as in Case I and found to be minus 8 mm. of mercury on expiration and minus 10.5 mm. on inspiration on the affected side. On the non-affected side the pressure ranged from minus 6 to minus 8 mm. of mercury.

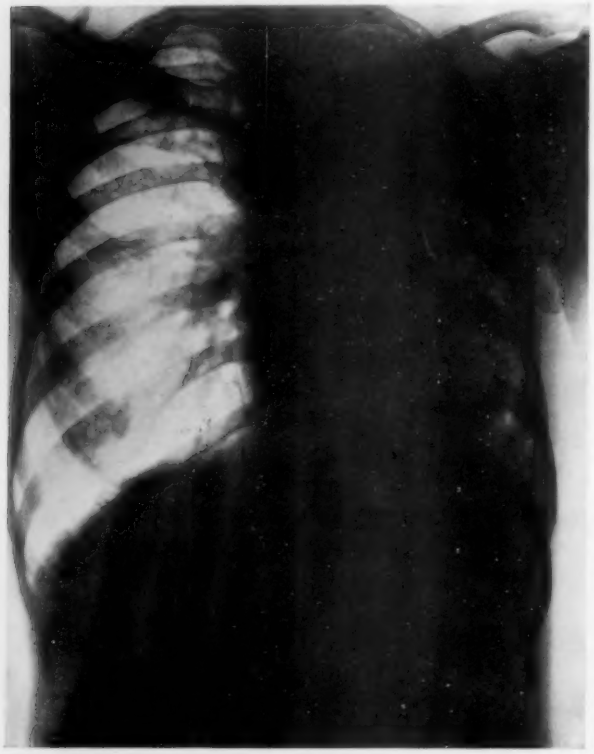

FIG. 4.—Case III. Röntgenogram showing atelectasis of the left lung due to metastasis from a fascial sarcoma of the thigh.

Three days later the left chest had regained its normal shape and the mediastinal structures had returned to their normal position. The resonance of the lung had returned and the breath sounds were normal.

Ten days later an open reduction of the humeral head was done under ether anæsthesia and was not attended by any pulmonary complications.

CASE III.—A. B., a negress of thirty-nine, entered the Emory University Division of the Grady Hospital, December 2, 1926. A year previously a small nodule had been removed from the posterior surface of the right thigh. In August, 1926, there was a recurrence of the growth, which was removed under local anæsthesia, and in November, 1926, a third excision was done. At the time of entrance to the hospital (December 2, 1926) there was a cauliflower mass about 8 cm. in diameter on the posterior portion of the right thigh just below the gluteal fold. It was partially necrotic and infected. (Biopsy showed a round-cell sarcoma.)

The patient had lost forty-five pounds since the onset of her illness a year before admission. The liver was enlarged and thought to be the seat of metastasis, although the edge was smooth. There were no other signs of metastasis except in the lungs.

On inspection the left side of the chest was definitely collapsed and the interspaces narrowed. On inspiration there was only slight movement on the left. The whole left lung was dull to percussion. The heart was displaced to the left side with the apex impulse in the sixth space, 2 cm. outside the mammary line. Breath sounds were weak and distant. The right chest was normal in every respect.

X-ray January 3, 1927, showed a definite atelectasis of the left lung with narrowing on the intercostal spaces and displacement of the heart to the left side (Fig. 4).

Estimation of the intrapleural pressure was made January 6, 1927. On the left side the pressure ranged from minus 11 mm. of mercury on expiration to minus 13.5 mm. on inspiration. The pressure on the right, or non-affected side, was practically the same.

Three other X-ray examinations of the chest were made, and all showed practically the same degree of collapse of the lung, but the amount of aëration varied to some extent.

It was thought that the atelectasis in this case was due to bronchial obstruction from a metastatic nodule.

At the time of discharge from the hospital, March 15, 1927, there was no change in the physical signs of the lungs.

Comment.—The presence of a marked reduction in the intrapleural pressure in three cases of massive atelectasis of the lungs is in keeping with the physical signs. The extreme displacement of the mediastinum toward the side of the lesion indicates a lowering of the pressure on the affected side, such as is found in no other pulmonary condition. The rapid pulse, cyanosis, and dyspnœa occurring in some cases may be due to mediastinal displacement. It is probable, therefore, that the introduction of air into the thoracic cavity in order to raise the pressure, and so bring the mediastinal structures back to their normal position, may be of therapeutic value.

CONCLUSIONS

1. Pulmonary atelectasis is not infrequently a post-operative complication, as is shown by the increasing number of reported cases.

2. There is a definite and well marked lowering of the intrapleural pressure as shown by the manometric readings in the cases here reported, and by the physical signs of mediastinal displacement and retraction of the ribs and intercostal spaces.

3. The estimation of the intrapleural pressure is advocated as a diagnostic method, since in no other condition is there a lowering of this pressure.

4. It is suggested that the introduction of air into the pleural cavity of these cases showing marked cyanosis and dyspnœa may be of therapeutic value in bringing the mediastinal structures back to their normal positions.

Since this paper was written another case of post-operative atelectasis has been observed in which the intrapleural pressure ranged from minus 11 mm. of mercury on expiration to minus 14 mm. on inspiration.

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CALCULOUS OBSTRUCTION OF THE COMMON AND HEPATIC BILE DUCTS*

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Most clinics in the past decade have witnessed a marked decrease in their general surgical mortality. The death rate in some diseases has been reduced so greatly as to be almost negligible, but in others, the most recent advances in operative preparation and technic have not been productive of such excellent results.[1] While remarkable progress has been made in the surgery of the biliary tract, the mortality and morbidity are unduly high in certain groups of cases, and calculous obstruction of the common and hepatic bile ducts still remains a formidable foe of the average surgeon. A case analysis of this particular group was undertaken with the hope that a free and open discussion might shed further light on the factors responsible for the high death rate.

This study is based on ninety-two cases of primary and twenty-two secondary cases of calculous obstruction of the common and hepatic bile ducts. These were gathered from one thousand, two hundred and eighty ward cases of gall-bladder and biliary duct disease exclusive of stricture and malignancies operated at the Mt. Sinai Hospital, New York, from 1917 to 1926. Eighty-five per cent. of these were accompanied by lithiasis, and nine per cent. of this number were complicated by the presence of stone in either or both of the common and hepatic bile ducts. A review of Table I will demonstrate that the presence of acute infection increases the mortality more than twofold, from 2.7 to 7 per cent., but when this is coupled with a calculous obstruction of the common bile duct, the death rate leaps to twenty-three per cent. (Table I.)

The gall-bladder in this group when present and visualized gave evidence of marked chronic inflammatory change in every case but one, a case of intrahepatic calculi. As a rule it was thickened, dull gray in color, often intimately adherent to adjacent viscera, occasionally completely hidden beneath a veil of firm dense adhesions. Recent acute inflammation was present in twelve cases. The size of the gall-bladder varied, larger than normal in half, and contracted in the remainder, with calculi absent in over a third of the cases.

Most common duct stones unquestionably originate from the gall-bladder where they are formed as the result of bile stasis, hypercholesteræmia and infection. A few maintain,[2] however, that the primary foci may be the smaller bile radicles of the liver. But the disease of the gall-bladder and its ducts are no longer considered isolated entities, but rather an expression of hepatic

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pathology. In fact, the degree of cholecystitis and cholelithiasis might be looked upon as a mirror reflecting liver change,[3] for all gradations of inflammation have been noted from leucocytic infiltrations of the smaller bile passages to acute yellow atrophy.[4] It has been shown that as a result of gall-bladder damage there is a tonic spasm of the sphincter of Oddi with a general hydrohepatosis[5] and atrophy of liver tissue with scar tissue replacement. In a third of the cases the liver was enlarged and in many cirrhosis was present. While the margin of safety of the liver is undoubtedly large,

TABLE I.

Summary of 1280 Operated Cases of Biliary Tract Disease. (Exclusive of Malignancy and Duct Reconstruction.)

Type of operation with percentage mortality	Diagnosis	No.	Percentage mortality		
Cholecystectomy in 1155 cases with percentage mortality of 3.4	Acute cholecystitis	85	4.7	Aver. % mortality 3.6	Average per cent. mortality 5.4
	Chronic cholecystitis	110	1.8		
Cholecystostomy in 11 cases with percentage mortality of 18.0	Acute cholecystitis and cholelithiasis	138	9.4		
	Chronic cholecystitis and cholelithiasis	833	2.7		
Cholecystectomy in 82 cases with percentage mortality of 23.1	Acute cholecystitis with common duct stone	1	0.0	Aver. % mortality 23.6	
	Chronic cholecystitis with common duct stone	35	40.0		
Cholecystostomy in 5 cases with percentage mortality of 20.0	Acute cholecystitis, cholelithiasis and common duct stone	11	18.0		
	Chronic cholecystitis, cholelithiasis and common duct stone	49	17.0		
	Common duct stone	18	16.0		

a certain degree of deficiency exists which is usually associated with renal incompetence. Frank cases of gall-bladder disease with azotemia and abnormal urinary findings should immediately suggest the probability of profound liver dyscrasia.

It is rather difficult to visualize the migration of calculi from the gall-bladder when the diameter and the spiral valves of the cystic duct are considered. These, in most instances, must reach the larger ducts in rather a small form, and these increase in size, aided by the products of biliary stagnation. The majority of these potential calculi are probably washed through the ampulla and rarely occasion clinical symptoms. In very rare cases, only twice in the series, liver calculi [6,7] may be the source of common duct obstruction, but this particular genesis must be extremely uncommon, excepting for some hepatic duct stones. Primary choledochal stone formation is most unlikely, especially when one considers the small number of common duct stones developing after the great number of cholecystectomies performed. In fact, most secondary operations for common duct calculi

prove that the surgeon was either directly or indirectly responsible for their presence by committing two omissive sins. Failure to properly probe and palpate the biliary ducts, and forcing small calculi through a patent cysticus while performing a retrograde cholecystectomy, account for practically secondary choledochal stones. In twenty-two secondary cases no evidence could be adduced to show that the calculi found were formed in the common bile duct with the exception of the soft pultaceous material made from inspissated bile in one case.

The degree of dilatation and the contents of the obstructed bile varied considerably. The diameter of the choledochus ranged from normal to that of the small intestine. The contents regularly showed no evidence of frank infection, although culture showed signs of bacterial activity. Pus was present only twice, and white bile once. The calculi varied from gravel to the size of hazelnuts, and from one to fifty in number. In eighty-four cases in which the stones were confined solely to the choledochus, the mortality reached twenty-one per cent., in twenty in which the hepaticus too was obstructed, the death rate was thirty per cent. In four instances of hepatic calculi there were no deaths. In forty-eight cases in which stones were solitary, the mortality was eighteen per cent., while in fifty cases in which they were multiple, the death rate was twenty-five per cent. While the degree of obstruction produced by a solitary calculus is not proportionate to its size, drainage naturally is obstructed more effectively and completely when multiple stones block several areas of the larger duct system of the liver. This increases back pressure and with it comes greater absorption resulting in increased toxicity, and higher mortality.

Jaundice, the main product of obstruction, was not always present, yet at some time in the course of the disease it complicated the majority of cases. When present it is equivalent to probable liver dysfunction, potential kidney injury and a variable degree of tissue devitalization. It means a general absorptive systemic poisoning through a retention of those waste products and bacteria ordinarily eliminated through the bile. This cannot be expressed clinically in terms of hemorrhage alone. Even though this factor can now be eliminated to a large extent, the mortality is still high because the indelible effects of irreparable tissue injury augmented by years of repeated insult remain.

It is amazing how long the average patient will endure the suffering of gall-bladder disease and tolerate purposeless medical treatment. The delay is costly, and the dangers of operation seem to increase directly with the length of time that surgery is postponed. The average number of weeks during which these patients complained of their symptoms was more than two hundred. In other words, they were ill continuously or intermittently for almost four years. Those who survived operative intervention suffered about three years, one hundred and seventy-five weeks, while those who succumbed delayed their operation for two hundred and sixty-four weeks, or more than five years. The deleterious effects of this intermittent bilirubi-

næmia and infection over prolonged periods are certainly illustrated by these statistics, and even more poignantly by those which follow. Cases which had a smooth convalescence were icteric nine days prior to operation, those which developed post-operative complications averaged eleven days of jaundice, and those which succumbed had been icteric twenty-four days prior to surgical intervention. The mortality in those with complete obstruction was sixty per cent., while the death rate of those in which jaundice was not apparent either clinically or chemically was nine per cent.

TABLE II.

Decade	Number	Deaths	Percentage mortality
20–29	9	1	11
30–39	25	4	16
40–49	30	7	23
50–59	35	10	29
60–69	14	4	29
70–80	1	1	100

TABLE III.

Sex	Deaths	Percentage mortality
Males 18	6	33
Females 96	21	22

Common duct obstruction in cholelithiasis is naturally more common among women and most frequent clinically during the fourth and fifth decades of life. These statistics, and the influence of age on mortality may be seen in Tables II and III. The history as a rule is one of gall-bladder disease characterized by upper abdominal distress and innumerable attacks of typical colic accompanied in most instances by the intermittent appearance of transient jaundice, dark urine, clay-colored stools, and more rarely by chills and fever. While the symptoms may exist for thirty years, or be as recent in onset as a week, the average period of complaint is about four years. In secondary cases, symptoms may recur from a few months to twenty-two years after operation, the average period being eight years. However, the appearance of pain often of a colicky nature, occasionally accompanied by jaundice, and less frequently by chills and fever, is not always indicative of common duct stone. Following any cholecystectomy, there is a certain degree of compensatory dilatation of the ducts,[8] probably an increase in the mucus, besides the infection still resident in the liver or pancreas, or both.[9] These are sufficient causes for the symptoms. In the period of 1917 to 1926, there were twelve cases, not included in this series,

admitted following cholecystectomy, complaining of the condition described. Eight cleared spontaneously with rest in bed and forced fluids, and four were discharged against advice. On the other hand, the absence of jaundice and its complications is no proof that the choledochus and its branches are free and unobstructed because more than eighteen per cent. of the patients gave no historical, physical or chemical evidence of icterus, and yet single or multiple ductal calculi existed. Icterus, however, was undoubtedly present at some time, but passed unrecognized. It was rarely progressive or intense, and in only five per cent. was the obstruction complete for a prolonged period. A deep icterus, increasing in intensity without pain should arouse suspicion as to the possibility of a carcinomatous occlusion arising in the choledochus,[10] ampulla of Vater, head of the pancreas or second portion of the duodenum. In this series, definite epigastric pain or right upper quadrant colic was present in one hundred and thirteen cases. One patient only gave a history of painless jaundice, but X-ray examination revealed a solitary calculus which operation confirmed as the cause of obstruction. Infection while probably universally present and insidious in its effects, did not always manifest itself clinically because biliary drainage was rarely completely blocked. Nineteen of the patients had temperature on admission and about twenty gave a definite history of severe shaking chills, but only a few presented the syndrome first described by Charcot. Infection severe enough to manifest itself by chills and fever is a grave complication and over fifty per cent. of these patients succumbed soon after surgical interference.

Physical examination showed the majority to be well nourished, only eighteen appearing as though they had lost weight, and about a third were described as "appearing acutely ill". It is this fair physical appearance which is most misleading, and constitutes the false threshold upon which most radical surgical intervention takes its footing. Jaundice usually of a mild degree was present in eighty-five and intense in only nine. The abdomen as a rule was soft and lax, in twenty-eight there was upper right quadrant rigidity of varying degree. The liver was enlarged in thirty-six cases and while the gall-bladder was reported as palpable in nineteen, exploration proved that only eight may have been sufficiently distended to be palpable, verifying the practical reliability rather than infallibility of Courvoisier's law.

The laboratory tests were not as important diagnostically as in determining operative indications and post-operative progress. The Meltzer Lyons test added but little in the differential diagnosis, and cholecystography because of its present dangers in the jaundiced was of small help. Liver function tests in these icteric individuals were found almost valueless. The Van den Bergh reaction which gave a quantitative estimation of the bilirubin in the blood was of inestimable value. The degree of jaundice is very deceiving clinically and this serum reaction readily sensitive to minute changes in the degree of bilirubinæmia, was a fairly reliable aid in judging its intensity. Its value as an indicator of obstructive and non-obstructive icterus was more academic than real. Bleeding and coagulation times usually prolonged

were extremely important as safeguards against hemorrhage, and a blood chemistry examination gave some indirect idea of liver and kidney function, but too much credence was never placed on normal figures for they were often found to be very misleading in the prognostication of the post-operative course.

The best time for operative interference always taxes surgical judgment. There is no doubt that patients are better risks when the blood bilirubinæmia is normal. There is always the possibility that the obstruction will be relieved spontaneously by the passage of the stone into the duodenum. In the ten-year period covered by this series, ten patients were provisionally diagnosed as suffering from calculous obstruction. The condition in eight subsided under conservative observation, the stone being recovered in the fæces of three. But the relief of obstruction clinically is no positive proof that the calculus has been eliminated because it may have subsided sufficiently to permit a freer drainage. If the degree of obstruction was constant or increasing as determined by daily Van den Bergh estimations, no time was lost in immediate exploration.

A routine standardized ante-operative preparation for these patients must now be regarded as paramount. Unfortunately, no plan of organized preparation was instituted in this series. The tissues should be liberally supplied with fluid, the alkaline reserve increased, and the liver sufficiently protected with glycogen through high carbohydrate diet, augmented, if necessary, by the rectal and intravenous administration of glucose solution. Should the sugar tolerance be low, it can easily be raised and controlled by the judicious administration of insulin. Hemorrhage usually can be effectively controlled by the use of calcium chloride intravenously,[11] supplemented, if necessary, by blood transfusion. This is excellent not only because it diminishes the tendency to bleed, but because it furnishes an internal stimulative meal.

In conditions such as these, inhalation anæsthesias have been repeatedly proven to be the added fatal insult.[12,13,14] There is no reason why these cases should not be satisfactorily explored under high spinal anæsthesia, and although the blood-pressure is apt to be low, it can be effectively maintained by hypodermic ephedrine. The few cases in this series operated under local abdominal wall block were usually the sickest, so that the mortality of 33 per cent. is no indication of the efficacy of this form of anæsthesia. (Table IV.)

TABLE IV.

Anæsthesia	Number	Deaths	Percentage mortality
Gas and ether	99	21	21
Gas and oxygen	3	1	33
Gas, oxygen, and ether	6	3	50
Local	6	2	33

The best operation for calculous common duct obstruction is the prophylactic. Each case of cholecystitis or cholelithiasis, whether presenting icterus or not, should be considered a potential choledocholithiasis. If the common bile duct and its branches were manually palpated in a routine way, the morbidity of recurrence would be greatly lessened. The choledochus should be explored especially when the gall-bladder and cystic duct contain many small stones, or the wall of the common duct is thickened, or a history of fever, chills, and icterus has been obtained, and in secondary explorations for pain following cholecystectomy. The advisability of probing the common duct in cases without a history suggestive of common duct stone is debatable, and it is barely possible that post-operative biliary leakage may come from a fistula inadvertently made by a fine probe penetrating the walls of the choledochus. It is true that the palpating fingers may not feel stones, especially in the retroduodenal portion of the choledochus, but the probe too may pass them unnoticed, as the autopsy protocols in six cases will certify. Calculi left behind are often responsible for death because biliary obstruction still continues. It must be stated, however, that no matter how carefully and skilfully the operator palpates, and sounds the bile channels with probe, forceps and spoon, calculi may be left behind. Another safeguard worth employing is the temporary ligature of a patent cystic before attempting a retrograde cholecystectomy for multiple small calculi as suggested by Dr. Edwin Beer.

A common duct with calculi is rarely difficult to locate and isolate at a primary operation, but it should be adequately exposed before it is incised. When once stones have been located they should be held, if possible, until extracted, because calculi slipping back into a hepatic may never be recovered again. This happened twice and once led to disastrous consequences. A supraduodenal incision is best and safest for the removal of most calculi and was used eighty-nine times. Some surgeons preferred to dilate the cystic and thus express small choledochal stones, and if this was impractical, the duct was split open into the common or hepatic. This was done in nineteen patients, but in one fatal hemorrhage resulted. While this procedure is regularly innocuous, it is possible to injure the right hepatic or an aberrant branch of the gastroduodenal artery. Large impacted calculi which cannot be delivered through a supraduodenal incision may be crushed as was done once, but lithotripsy is quite apt to damage mucous membrane and fragments may remain to form nuclei for future stones. An impacted ampullary calculus occasionally may be forced into the duodenum, but a safer course is an adequate exposure of the retroduodenal portion of the duct by a Kocher mobilization so that the stone may be pushed supraduodenally and there extracted. If this is not feasible, an anterior duodenotomy, which was only necessary twice in this series, is preferable to a retroduodenal choledochostomy. There is always danger in this procedure of pancreatic duct injury and retroperitoneal infection from leakage, while a duodenum carefully

sutured with the choledochal drainage kept away from the suture line, rarely results in fistula.

The question of common duct drainage is still debatable. It may either be completely sutured, or drained internally or externally. Each of these procedures has its strong adherents—each method claims the best results.

Dilatation of the ampulla followed by a complete suture of the common duct without drainage,[15] while apparently ideal, seems a dangerous procedure at best. It has been stated that the removal of drainage is likely to be followed by hemorrhage, that the loss of bile is detrimental to many, and that these wounds heal by secondary intention [16]—yet all of these conditions even if they do arise can be more effectively combated than a biliary peritonitis from leakage. The danger of acute biliary suppression from a too rapid and continued decompression of a distended duct system [17] arises more frequently in academic discussion than in clinical experience, although the conditions obtaining here are quite similar to those of urinary suppression following a suprapubic cystostomy for urethral obstruction. Suture of the choledochus with drainage to the suture line seems to possess no advantage to choledochostomy. If the region of ampulla has been probed, the reflex spasm of the sphincter of Oddi, together with the œdema and exudation incident to trauma, is almost sure to produce complete obstruction. The sutured duct soon yields to the increase of intraductal pressure and the presence of infection. Some surgeons have added internal drainage to primary suture to overcome this sphincteric spasm.[18] After dilatation of the ampulla with graduated bougies, a drainage tube is passed from the hepaticus into the duodenum, leaving the distal extremity sufficiently long so that it will eventually be removed by intestinal peristalsis. The method, while ideal as far as primary union of the duct and drainage of bile is concerned, seems open to too many possible complications if tube reconstruction of the biliary tract may serve as an example.

External drainage not only gives free vent to the products of the inflamed radicles of the liver, thus allaying the cholangitis, but it rests the pancreas, and if the retrojection of bile is responsible for some grades of pancreatitis, then that organ too shares in the benefit derived. Moreover, the opening of the choledochus is a safety valve through which additional calculi may be extruded, if any inadvertently remain. Stones were discharged in this manner in four cases.

When all angles of the drainage problem are considered, the external method whether used *via* the cysticus, choledochus or hepaticus, although imperfect, is the safest, and its end results are not bad enough to justify the more radical and dangerous procedures recently advocated.

The problem of the diseased gall-bladder, in any primary operation for calculous obstruction is a difficult one, because cholecystectomy is ordinarily indicated here as in most other cases. In this series of 1280 cases, the gall-bladder was removed in over 95 per cent. of the patients, and in about 85 per cent. of the ninety-two primary cases of common duct obstruction. But

there should be no routine procedure; each case should be decided individually. The reason for leaving the diseased gall-bladder is not that it may be necessary for anastomotic purposes should the choledochostomy result in stricture. This rarely happens if the common duct is drained properly. But presence of jaundice is the danger signal even though the patient may appear in good condition. It immediately converts a standardized routine procedure into an emergency which demands the simplest drainage operation to relieve the jaundice, choledochostomy. A dilated duct is usually easily identified, the calculi are ordinarily extracted without difficulty and a drainage tube inserted, but if this seems inadvisable because of technical difficulties or the precarious condition of the patient, cholecystostomy if the cystic is patent, must answer. An additional cholecystectomy while only adding fifteen to twenty minutes to the operating time, adds much more to the surgical shock, the possibility of hemorrhage and the likelihood of infection. It is this very triad which is responsible for most deaths. In the jaundiced, the oozing from the bed of denuded liver, while not sufficient to result in severe hemorrhage, contributes heavily to a stormy convalescence,[19] and the toxæmia increased by further absorption through the open lymphatics, is often sufficient to turn the tide against the patient. These gall-bladders which in thirty-five cases did not contain stones and were usually shrunken and atrophic, represented the end result of the local disease, and probably reflected the maximum of liver and kidney injury. The mortality in this particular group was 40 per cent. As far as the organ itself was concerned, it was silent; its removal was of little clinical importance but the cholecystectomy undoubtedly contributed to this fearful mortality. In a group of twenty-two secondary cases, simple choledochostomy was done in twenty-two and cholecystectomy added in only four. The mortality here was fourteen per cent. In spite of the fact that these secondary operations are technically more difficult because of the widespread and dense adhesions, shock and postoperative complications appeared less. The omission of cholecystectomy with its incident operative dangers may have been the dominant factor causing this decrease in operative mortality. Should future symptoms develop from a gall-bladder which was left, a subsequent operation can be undertaken. The multiple stage operation is never an indictment against surgical courage, or judgment. It certainly should be given a greater place of prominence in cholelithiasis complicated by common duct obstruction.

The causes of death in twenty-seven cases may be divided into the immediate, the intermediate, and the late. Shock and hemorrhage comprise the first, infection with hepatic and renal insufficiency the second, peritonitis, pneumonia and pancreatic asthenia the third. Twelve patients died of shock complicated in three instances by hemorrhage. Almost forty-five per cent. of deaths were due to an operative procedure of too great a magnitude under existing conditions. Eight deaths resulted from infection coupled with hepatic and renal insufficiency, a condition formerly known as cholemia. Six

succumbed to a peritonitis, and other complications such as pneumonia and embolism.

The post-operative course was uneventful in about sixty patients, and stormy in twenty-seven. The complications were caused by the effects of moderate liver and kidney insufficiency, resulting in persistent vomiting "cholemic" hemorrhages, oliguria and occasionally anuria with azotemia. The increase of jaundice noted in some was probably due to the further embarrassment of liver cells occasioned by the inhalation anæsthetic plus the operative manipulation spreading infection. Several of these cases were really resurrected by the judicious use of blood transfusions and the administration of sufficient amounts of saline and glucose solutions. The drainage of bile usually began during the first twenty-four hours, increasing materially the second and third days. The choledochostomy tube was usually free in about ten days for the T or L tube of Kehr [20] was never employed. Bile continued to drain ordinarily until the twenty-first to thirtieth day. In six cases in which the duct was primarily sutured, there was leakage, and thirty days intervened before the biliary drainage ceased. Fifty-eight cases in which the tube was placed in the choledochus were free of bile in twenty-eight days and the fifteen cases in which hepaticus drainage was used were dry in twenty-one days. Biliary drainage was regularly non-irritating, and pancreatic ferments were found in the two cases in which a dermatitis of the abdominal wall was present. Inasmuch as carmine crystals given orally did not appear in the wound, it is safe to assume that these were not cases of duodenal but rather pancreatic reflux. The rarity of this complication may be explained by recent anatomical investigations[21] in which it was exceedingly uncommon for the contraction of the muscle fibres in the region of the sphincter of Oddi to convert the common bile duct and the duct of Wirsung into one continuous channel.

Biliary fistulæ as a rule closed in about a month and coincidentally the stools, which were very acholic until then, assumed a dark brown color. Any fistula persisting over eight weeks should make one suspicious of a duct blocked by stone or one accidentally divided at the time of operation. It is still too early to estimate the value of X-ray examination of a biliary sinus injected with lipiodol. In one recent case, not in this series, in which a sinus persisted for more than six weeks, the lipiodol demonstrated quite effectively the biliary tree with the common very much dilated and a blockage in its distal portion just before it entered the duodenum. This was interpreted as due to a stone. Secondary operation revealed a patent duct. The factor of sphincteric spasm was overlooked, and the sinus subsequently closed spontaneously. Four cases which developed a persistent biliary sinus lasting over two months, were reoperated, in two of them calculi had been left behind, and in two the duct had sloughed, necessitating tube reconstructions. Conclusions: The mortality of calculous obstruction of the common and hepatic bile ducts in a series of one hundred and fourteen cases was twenty-three per cent. The figures are not unique for this hospital,[22,23] but represent

the mean obtained in other institutions both here and abroad. This is a sad commentary on medical practice and surgical procedure. As long as the laity in general are induced by the profession at large to procrastinate and temporize and delay surgical intervention until years of transient jaundice and continuous infection have irretrievably devitalized tissue, so long will this mortality be high. And, until surgeons realize that inadequate ante-operative preparation coupled with inhalation anæsthesias and radical one-stage procedures are responsible for their prohibitive death rate in these handicapped patients, the treatment of common duct stone will remain a barrier to the progress of the surgery of the biliary tract.

The author wishes to extend his thanks to Dr. Edwin Beer, Dr. A. A. Berg, Dr. Charles Elsberg, Dr. Howard Lilienthal and Dr. A. V. Moschcowitz, for the privilege of studying these cases on their respective services.

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STRANGULATED NON-PARASITIC CYST OF THE LIVER

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and

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The following case is reported because of the rarity of non-parasitic cysts of the liver and because it presents features not hitherto recorded.

M. P., age twenty-six, was admitted to the U. S. Veterans' Hospital, July 21, 1926, complaining of nausea and vomiting which began the day before. He had some discomfort in the abdomen but no severe pain, although the nausea and vomiting was quite marked.

In the past history there was a diagnosis of pulmonary tuberculosis with two previous hospitalizations. He had noticed a gradually enlarging painless movable tumor in his abdomen for about two years and had been told that its removal would cause death.

On examination a mass was found in the umbilical region extending downward to the brim of the pelvis measuring about 10 x 12 cm. This mass was slightly sensitive. The cæcal region was also sensitive but no muscle spasm or rigidity existed. The tumor could be moved laterally in each direction for a distance of 5 to 7 cm. It was smooth in outline and felt quite firm. The temperature, pulse, urinalysis and blood count were normal.

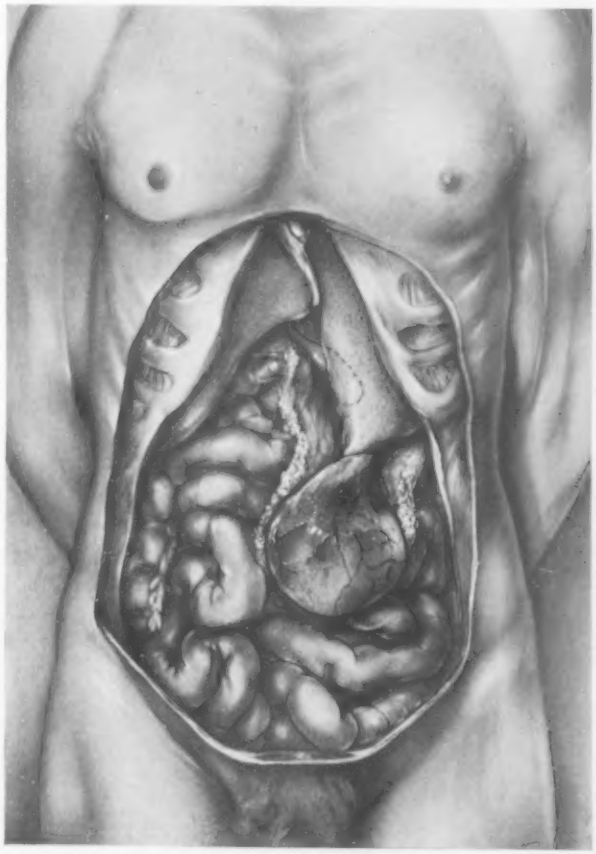

Fig. 1.—Appearance of cyst with its pedicle twisted.

Soon after admission to the hospital the nausea and vomiting ceased and because of this improvement it seemed advisable not to operate at once. Two days later vomiting recurred and the abdominal mass became more tender. He was not, however, considered very ill and operation was postponed until the fifth day of his illness, when it became obvious that exploration was necessary.

Operation.—A left rectus incision was made over the tumor. A dark colored mass

presented with slightly adherent omentum and intestines at the sides. It was found to be attached to the left lobe of the liver by a flat pedicle which was twisted to the right. (Fig. 1.) Beneath the pedicle was found a slightly thickened gall-bladder that was somewhat elongated and drawn downward from its normal position.

The mass was found to be a strangulated cystic tumor which was easily lifted into the wound. With interrupted chromic sutures the flattened pedicle was transfixed and ligated and the cyst removed. The appendix was also removed and the wound closed without drainage. Recovery was prompt and uneventful.

FIG. 2.—Detailed appearance of cyst.

The tissue was examined by Dr. H. R. Wahl, Professor of Pathology, University of Kansas, who reports as follows:

Gross Pathology.—Specimen consists of a large fluctuating cyst measuring about 15 cm. in diameter. (Fig. 2.) Light can be partly transmitted. There is a rather flattened pedicle 3 by 1 cm. composed of dark red friable tissue apparently of hepatic origin. This pedicle is flattened out over the surface of the cyst and is rather prominent over an area of 4 by 5 cm. On section of cyst, contents consist of a mass of soft light grayish gelatinous material. The wall of the cyst measures 2 to 3 mm. in thickness. Its inner surface is fairly smooth with a few ridges and with a few slightly discolored plaques over its lower end. The outer surface is smooth and glistening and shows rather prominent vessels.

Histological Pathology.—The section (Fig. 3) shows a laminated wall composed of alternating layers of red blood-cells and fibrous tissue containing many proliferating bile ducts embedded in a rather cellular stroma. The cyst wall itself is lined with a thick wall of fibrous tissue on the inside of which there is a layer of swollen cuboidal epithelial cells which resemble the cells lining the bile ducts. Within this layer there is some hemorrhagic eosin staining material containing a few nests of red blood-cells. Lymphoid cells are scattered about the proliferating bile ducts. There is some liver tissue flattened out over the surface of the cyst showing marked pressure atrophy and consisting, as noted above, of proliferating bile ducts and fibrous tissue. Only here and there are a few nests of liver cells seen showing fatty degeneration. The wall of the cyst in some places shows deposits of calcium corresponding to the discolored plaques noted in the gross.

Diagnosis.—Strangulated retention cyst of liver.

In 1923, J. F. X. Jones [1] reviewed the literature and collected 61 cases, including his own, of non-parasitic cysts of the liver that had been subjected to operation. Since then Schraack [2] has reported 6 cases not mentioned

by Jones, Maes [3] two cases, Alexander [4] one case, Burns [5] one case, Sims [6] one case, and Metz [7] two cases, making with ours 75 cases which have been operated upon. Jones quotes a letter from Dr. S. W. Harrington [8] of the Mayo Clinic, dated July 18, 1922, in which he states that 25 cases of multiple cysts of the liver had been observed at that Clinic. Only three of these were found when the operation was done for tumor or cyst of the liver. The remaining 22 were discovered at operation for gall-bladder disease, ulcer of the stomach and carcinoma of the stomach.

Jones has collected the opinions of several authors and has decided that non-parasitic cysts of the liver are best classified as: 1. Teratomatous or embryomatous cysts. 2. Pseudo-cysts. 3. Lymphatic cysts. 4. Cystic degeneration of the liver with cystic kidneys. 5. Cysts which arise from blood-vessels. 6. Cystadenoma. 7. Ciliated epithelial cyst. 8. Retention cysts.

FIG. 3.—Microphotograph showing details of cyst wall. 1. Cuboidal epithelium lining cyst. 2. Dense fibrous tissue. 3. Hemorrhage in cyst wall. 4. Proliferating bile ducts.

The determination of the etiology and proper classification in many cases is very difficult. Such cysts are, however, usually quite easily distinguished from the more common echinococcus cyst by the characteristic contents of the latter.

The clinical diagnosis of simple non-parasitic liver cyst is seldom made. If large enough to produce symptoms it is usually mistaken for gall-bladder disease, ovarian cyst, pancreatic cyst, mesenteric cyst or echinococcus cyst. In our case liver cyst was not suspected. We did not even determine that the tumor was cystic but suspected a solid tumor of the mesentery or gut or perhaps a floating spleen.

A retention cyst such as is here recorded is due to the engorgement and dilatation of a bile duct. Just why or how a duct becomes obstructed is not always easy to determine. Calculi and cicatrices have been mentioned as causes. Jones states that it is possible that an unrecognized irritation has caused swelling and hypersecretion in a bile duct, with occlusion of its outlet. Both the pedicle and wall of the cyst in our case showed marked fibrous changes. There was no gross evidence of any general cirrhotic changes in the liver above the pedicle.

The treatment of single non-parasitic cysts of the liver is total removal or marsupialization. In many cases they are so extensive and involve such a large portion of liver structure that removal is too dangerous. Good results have been reported after marsupialization and packing with gauze.

CONCLUSION

1. A pedunculated strangulated non-parasitic cyst of the liver is here reported. It is probably the first recorded.

2. Solitary non-parasitic cysts are rare and usually not diagnosed as such.

3. If symptoms are present operation is indicated. Total excision and marsupialization are the operations of choice.

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THE HEALING PROCESS OF GASTRIC ULCER IN MAN*

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Clinical and pathologic observations have long revealed that certain gastric ulcers heal, but the actual mechanism of the repair and the anatomic factors involved have not been completely analyzed in man. Recent studies of the reparative changes found in experimentally produced peptic ulcers,[24] and in ulcers of the stomach [8] and duodenum [19] in man have demonstrated the usual sequence of events. The present study includes observations of the gastric ulcers resected from thirty patients at the Mayo Clinic. Twenty-three of the patients were on pre-operative regimen before operation because of local or general complications, chiefly obstruction, hemorrhage, gastritis or dehydration. Six patients were studied who had not received medical treatment for ulcer for at least six months before operation. One patient was on strict medical treatment for two weeks before operation was performed.

LITERATURE

Rokitansky, and later Hauser, believed that the mucosa destroyed in an ulcer of the stomach extending down to the submucosa was repaired, for the most part, by contraction of dense fibrous connective tissue in the base of the ulcer. Hauser and Virchow emphasized the importance of circulatory disturbances (thrombosis, embolism and endarteritis) in the chronic course and in the healing process of peptic ulcer. MacCarty, in 1910, observed epithelium growing from the margin of an ulcer apparently in an attempt to cover the denuded crater. Bolton, in a series of experiments and clinical studies of gastric ulcer, noted that healing in gastric ulcer advanced by several steps: the separation of the necrotic slough in an ulcer base, then the covering of the defect by healthy granulation tissue. The epithelium from the margin of the lesion grew out as a single layer of flat cells which became cuboidal. Glands beginning as a single invagination gradually burrowed into the cellular stroma and formed a new mucous membrane. In the meantime the edges of the ulcer approached one another by contraction of granulation tissue.[1, 17, 33, 34] Askanazy believed with others that in many instances small erosions or acute ulcers heal and disappear as such. Robertson and Hargis from 2000 post-mortem examinations found 141 gastric ulcers, twenty-nine (approximately 21 per cent.) of which were healed.

The cycle of experimentally produced peptic ulcer in animals has been thoroughly studied and described by Mann and his co-workers,[23, 24, 26] from

* Abridgement of thesis submitted to the Faculty of the Graduate School of the University of Minnesota, on partial fulfillment of the requirements for the degree of Master of Science in Pathology.

the first break of the mucosa with hemorrhage and destruction of epithelium to the covering of the scar-filled defective area. To produce peptic ulcers experimentally Mann substituted a loop of jejunum for the duodenum at the pylorus with drainage of the duodenal contents into the ileum by entero-anastomosis. Promptly after this procedure chronic peptic ulcers developed in the transplanted jejunum. By laparotomy with inspection of the lesions at varying intervals after the primary operation, the approximate time of formation of the ulcer was determined. Frequent inspection and

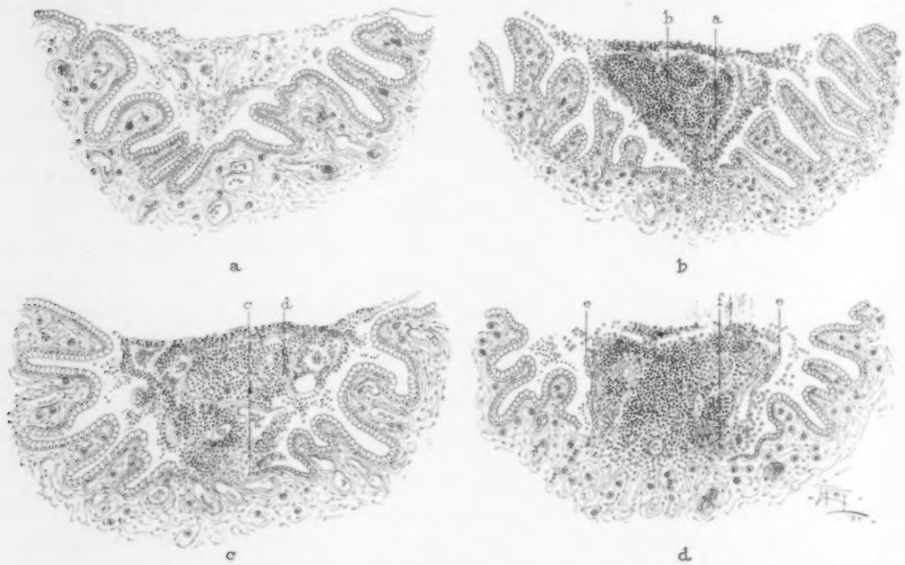

FIG. 1.—The stages of healing of gastric ulcer. a, healed edge of the ulcer; b, (*a*), break of the mucosa of the base of the ulcer, (*b*), blood clot in the defect; c, (*c*), flattened epithelium growing in from the edge of the ulcer, (*d*), formation of a mushroom of granulation tissue in the defect of the mucosa; d, (*e*), cuboidal epithelium attempting to cover the plateau of granulation tissue in the ulcer, (*f*), recent hemorrhage, with a break of the epithelium covering the base of the ulcer.

biopsy of the lesions after gastro-enterostomy illustrated all stages of healing, as well as the time required for complete repair.

To encourage the healing of experimentally produced chronic peptic ulcers Mann occluded the pylorus and drained the stomach by gastrojejunostomy. Anastomosis of the duodenum and jejunum near the site of the ulcer brought about healing in some animals, but the repair was usually slower than with gastrojejunostomy. In the healing of experimentally produced peptic ulcers, when the lesion was completely protected, hemorrhage into the crater of the ulcer rarely occurred. In observations on healing peptic ulcer in man hemorrhage was almost constantly noted, probably because the lesions were unprotected. The extravasation of blood into the cleft of the ulcer was not necessary for healing and at the time of the hemorrhage it probably interfered with the healing process. Granulation tissue grew from the base of the ulcer into the cleft to form a "mushroom" of capillaries and inflammatory cells. Epithelium as a single flat layer grew out from the margin of the lesion up the stalk and over the top of the granulation-tissue mushroom in

the cavity of the ulcer. After the denuded area had become covered and the lesion had healed, the fibrous connective tissue contracted with the formation of deformed and cystic glands so that the final result of healing was a scar-filled excavation covered by atypical epithelium. Mann [24] has found this peculiar granulation tissue plateau or mushroom in experimentally produced peptic ulcers that were healed or partially healed. He found that peptic ulcers of the most chronic perforating type were constantly attempting to heal and that granulation tissue was persistently attempting to form in the cavity of the ulcer. He had also observed a single layer of epithelium trying to bridge a perforating peptic ulcer closed only by omentum.[25] Epithelial cells creep out in this insecure position only to be swept off and destroyed; thus incessant battle between the forces of repair and destruction is carried on.

Morton recently found that excision of bits of mucosa from the stomach following "duodenal drainage operation" after the method described by Mann, was followed by the formation of true chronic ulcer in approximately half of the experiments. The ulcers occurred chiefly along the lesser curvature of the stomach and healing was always delayed.

Wolfer produced experimental ulcers in the stomach by irradiation of the mucosa. The ulcers healed spontaneously in from two hundred to six hundred days.

Kennedy found a duodenal ulcer in a child three days old who had died from melæna neonatorum. The healing changes, observed previously by Mann, were present. I have described similar healing processes in a gastric ulcer removed at operation (Figs. 1, 2, 3, 4, 5, 6); and Crohn and his associates [9, 10] have made similar observations.

The summation of studies on experimentally produced peptic ulcer in animals and gastric ulcer in man establishes the fact that repair occurs in these lesions, with some variations in the sequence and type of pathologic changes. The first prerequisite for healing of gastric ulcer is that the base shall be vascular enough to support granulation tissue,[15] and obviously the larger and deeper the excavation the longer the time required for healing. Early in the formation of the ulcer there is hemorrhage of the mucosa and sometimes of the submucosa and muscularis. There is solution of continuity of the mucosa with necrosis of tissue in the area of the lesion. The necrotic material is replaced by granulation tissue which develops in the base of the ulcer and fills or partly fills the excavation. The epithelium at the edge of the ulcer apparently becomes hypertrophic and hyperplastic. A single layer of flat to cuboidal epithelial cells creeps out on the granulation tissue in the base of the lesion,[23, 24, 26] and when the granulation-tissue bud later contracts the completely healed ulcer is observed as a scar-filled defect covered by irregular folds of epithelium with atypical glands, especially at the margin of the lesion. These glands are lined by cuboidal to columnar cells. Depending on the depth of the excavation the fibrous connective tissue may extend through submucosa, muscularis or down to the serosa. Hauser observed that

the muscle bundles at the edge of an ulcer were pulled up into the base of the lesion and replaced by connective tissue. The scar-filled cavity of the ulcer is not so plentifully supplied with blood-vessels as even the unchanged gastric wall, for the contraction of the granulation tissue markedly interferes with the blood supply.[15] This contraction, together with the atypical epithelium, renders the healed area a point of low resistance, ulceration therefore at the site of the original lesion is not uncommon.[9, 15]

FIG. 2.—Flattened epithelium covering the granulation tissue in the edge of an ulcer (× 50).

Obviously there are many exceptions to this manner of healing because of the continued activity of traumatic factors. Epithelium at the edge of the lesions may be torn loose from the granulations in the base. In large ulcers the epithelial cells may grow well out on the base of the excavation while the network of blood-vessels in the centre of the lesion is torn loose by traumatic agents and reformed again and again. If the capillaries are torn they bleed and this bleeding retards healing. Blood clot may organize and granulation tissue develop again from the base of the ulcer and epithelium will attempt to cover the plug in the cavity of the ulcer.[8, 23, 24, 26] A lesion may show healing changes in one area and ulcerative destructive changes in another.

METHOD OF INVESTIGATION

All ulcers were put in 10 per cent. formalin solution as soon as removed. It is important not to wash the tissue to be examined since exudates, blood and granulation tissue in the cleft of the ulcer might easily be torn off and washed away. Serial sections were made of all the ulcers and they were stained with hæmatoxylin and eosin. The entire diameter and edge of the lesion were included in the preparation unless the excavation was too large for section; there the ulcer was cut in two and preparation for microscopic study made from one portion.

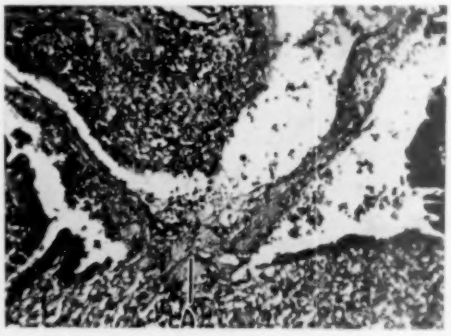

FIG. 3.—Break in the mucosa at (*a*) with organizing hemorrhage in the defect (× 120).

Pre-operative treatment was advised for twenty-three of the patients in order to combat or relieve complications, especially to overcome dehydration, to reduce gastritis, to allow recovery of muscle tone after gastric retention, to allow a period of recovery from the fatigue of necessary examination, to treat hemorrhage, and relieve retention and vomiting. If a patient

had gastric retention he was kept on a regimen which consisted of two-hour feedings of 200 c.c. of liquid from 6 A.M. to 8 P.M. Liquid food was given since it is quickly and easily assimilated and it can be removed by stomach tube. Fifteen hundred cubic centimetres of 5 per cent. glucose solution was given every twenty-four hours by proctoclysis. The stomach was washed out once or twice daily as seemed necessary and if the patient was dehydrated intravenous injections of glucose and sodium chloride were given. Bleeding from an ulcer was usually managed by rest in bed and transfusions of blood. If retention was not found at examination the hospital care consisted of that usually given in cases of ulcer for a varying number of days. The resected ulcers from six patients who had not previously been treated for ulcer within six months of their pre-operative preparation were also studied. One patient, a physician, with a short history, was maintained under strict medical management for ulcer for two weeks.

RESULTS

It is fully realized that there are many obvious variations of the sequence of events in the healing of gastric ulcers as outlined, but the steps recorded are those generally found in lesions with healing changes. One of the most common variations in these steps is that the first and second may be interchanged. The action of traumatic agents may cause other differences, as has been mentioned.

In the healing lesions (as determined by the foregoing criteria) the growth of a single layer of epithelial cells from the margin of the ulcer was a stubbornly persistent almost constant factor in repair. This mechanism was present to a greater or less extent in almost every case regardless of the size of the lesion, its duration or the previous treatment. Even if the soft spongy base usually seen in ulcers was replaced by fibrous tissue, the epithelium at the margin attempted to grow out as a single flat layer of cells and covered this denuded area.

The granulation-tissue mushroom which developed in the base of healing peptic ulcers was the keystone of the reparative process. It was found in healed or partially healed experimentally produced peptic ulcers.[24, 25] Kennedy and others[8, 9, 10] have noted its presence. If for any reason this granulation-tissue bud or tuft could not form, or if it formed and could not be maintained in the crater of the ulcer, the lesion remained unhealed indefinitely. I have not found a true ulcer completely healed by epithelial outgrowth from the margin alone. The plateau of granulation tissue must form in the base of the ulcer. Erosions of the mucosa healed as did ulcers. The epithelium grew out on the capillary network which exhibited plateau-like overgrowth. In large ulcers (approximately 1 cm. in diameter and larger) in which a single granulation-tissue mushroom apparently could not form or survive in the crater, many small granulation-tissue buds were sometimes observed scattered in the cavity and particularly in the margin of the ulcer. (Fig. 7.) The smaller tufts had all the characteristics of the larger ones.

They were soft, spongy masses of capillaries and young connective tissue and the epithelium attempted to cover them. (Figs. 8 and 9.) In the whole series no ulcer was found which had healed completely by the formation of granulation-tissue mushrooms either at the margin of the ulcer or in the cavity.

The epithelial cells which cover an ulcer or an erosion are atypical and undifferentiated. At the edge of gastric ulcers Askanazy noted cystic glands, goblet cells and, less often, delomorphous cells. In some cases he found epithelial desquamation or caruncle. Partially healed gastric ulcers and healed erosions in stomach of man have been studied to determine whether this regenerated epithelium recovered its functional activity. The technic employed was described by Harvey and Bensley and used by them and others [11, 37] in observations on the origin and production of the hydrochloric acid of gastric juice. Using indicators, chiefly neutral-red solutions, Harvey and Bensley were able to demonstrate acid reaction in the foveolæ of the gastric glands of experimental animals. The parietal cells were alkaline in reaction and it was concluded that the acid of the gastric juice was not formed in the parietal cells as such, but was probably produced in the foveolæ of the gastric glands and on the surface of the gastric mucosa. I have employed neutral-red solutions (1:1000, 1:2000, and 1:10,000) applied to small bits of fresh mucous membrane snipped off as described by Dawson and Ivy from partially healed ulcers or erosions. These preparations were observed through a microscope. Razor sections, after the method used by Terry, were also made from healed or partially healed gastric ulcers and erosions and stained in a like manner with neutral-red solutions. The epithelial cells covering or partly covering an ulcer or erosion stained yellow (alkaline reaction). Occasionally a few cells were noted that stained orange-red (neutral reaction). None of the epithelial cells covering the surface of a partly healed ulcer or erosion stained red. The mucus and the secretion on the surface of the stomach and in the base of the ulcer was the crimson of acid

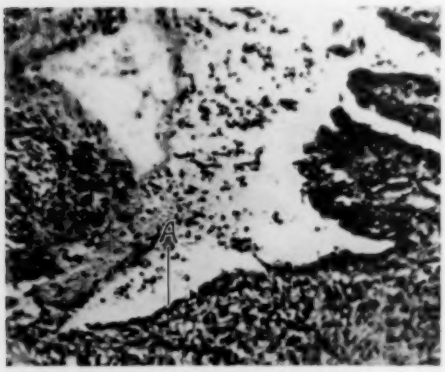

FIG. 4.—Flattened epithelium at (*a*) growing from the edges of the ulcer on the granulation tissue in the base of the defect (× 120).

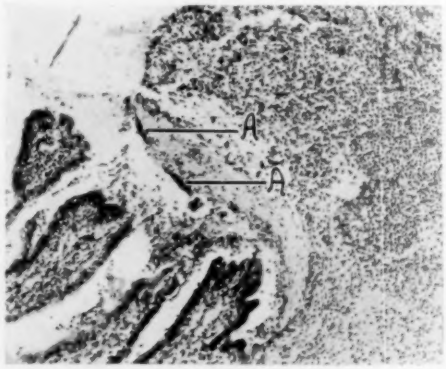

FIG. 5.—Epithelium along the edges of mushroom of granulation tissue at (*a*) (× 80).

reaction. Gastric glands from fresh resected specimens at some distance from the ulcer were studied with the same technic. The parietal cells (which are not plentiful in the pars pylorica [29]) when exposed to neutral-red solutions stained yellow as previously recorded by Harvey and Bensley. Occasionally a parietal cell was found that stained orange-red.

Dawson and Ivy recently repeated a portion of Harvey and Bensley's work, using dogs with Pavlow pouches. They snipped off bits of gastric mucosa from the gastric pouch while the mucosa was actively secreting and within two minutes the mucosa was prepared with neutral-red solution and observed under the microscope. Three distinct types of reaction were found in these preparations. Within the first few minutes the parietal cells, canaliculi of these cells and foveolæ of the gastric glands stained crimson, indicating a hydrogen-ion concentration on the acid side of neutrality. This red color in the cells was quickly displaced, usually within two minutes, by the orange-red of neutral reaction which passed over to the yellow of alkaline reaction. The alkaline tint persisted for as long as twenty minutes when it changed to the red of acid, indicating the death of the cells. The observation of the first acid reaction was essentially the only difference between these results and those obtained by Harvey and Bensley. Dawson and Ivy believed that the first acid reaction was due to the presence of free hydrochloric acid in the parietal cells and foveolæ of the gastric glands and that the second stage of alkaline reaction was probably due to the cessation of acid formation which in turn was due to the excision and to diffusion of acid from the cells. These observers accounted for the difference between their results and those of others by two factors: the material they used was obtained from actively secreting mucosa, and no unphysiologic procedure (such as stunning, bleeding to death, or anæsthesia which are known to inhibit or abolish gastric secretion) preceded excision of tissue for study. In our studies the material was always obtained during operation and the patients were under the influence of a general anæsthetic.

The epithelium covering a partly healed or recently healed gastric ulcer or erosion appeared to be of a regenerative type rather than concerned with secretion. The fact that no acid was demonstrated in the cells by this method was subject to the same criticism as that made by Dawson and Ivy of the work of Harvey and Bensley. Morphologically the epithelial cells covering gastric defects soon after healing were atypical round or oval cells [32] with the nucleus near the centre in contrast to the columnar cells on the surface of the gastric mucosa.

In this series of cases multiple ulcers were frequently found. Judd and Proctor reviewed operations on the stomach performed at the Mayo Clinic in a ten-year period and found that multiple gastric ulcers were present in 6 per cent. of the cases. Since resection of portions of the stomach is becoming more and more common there is every reason to believe that multiple ulcers of the stomach will be found more often. Robertson and Hargis, reviewing post-mortem material, found that in approximately 30 per cent.

of cases of gastric ulcer the ulcers were multiple. In the present series of thirty cases, in fourteen (approximately 46 per cent.) the ulcers were multiple. In a few instances there were ulcers in both the stomach and duodenum.

The entire series of gastric ulcers automatically arrange themselves into three groups: (1) Active unhealed (chiefly the perforating type), (2) recurring, and (3) partly healed. Ulcers designated as perforating were those in which destructive excavation predominated and the chief characteristics were the deep steep-walled ulcer craters. Obviously all ulcers have such characteristics, but in some they are more striking and conspicuous in contrast to lesions in which marginal encroachment of the process seems most prominent. Another ulcer not infrequently noted was of a chronic type and apparently had assumed a perforating form, that is, there was a V-shaped or U-shaped area of necrosis usually in the centre of the crater. This apparently was a recent development in an already established chronic ulcer. In the thirty cases comprising the series studied there were ten ulcers that were classified as perforating. The steep-walled craters were poorly covered by epithelium and usually only necrotic material and fibrous connective tissue were found in the base. Soft spongy granulation tissue was demonstrated only a few times in the cavity of the ulcer. Thrombosis of the arteries and in many cases of the veins was often found in the base of perforating ulcers. Endarteritis was present many times deep in the gastric wall beneath a perforating ulcer. The interference with blood supply which apparently was a feature of these lesions was perhaps a factor in the failure to heal and in the etiology.[40] In some cases of large chronic ulcers which showed a tendency to perforate near the centre, marked arterial changes, chiefly thrombosis or endarteritis, were demonstrated. Obviously healing did not occur near the middle of these ulcers.

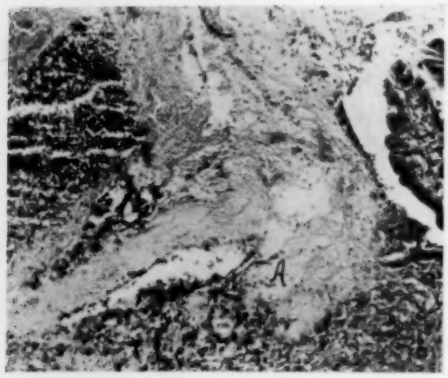

FIG. 6.—Fresh hemorrhage at (*a*) with a sharp break in flattened epithelium and loosening of granulation tissue (× 100).

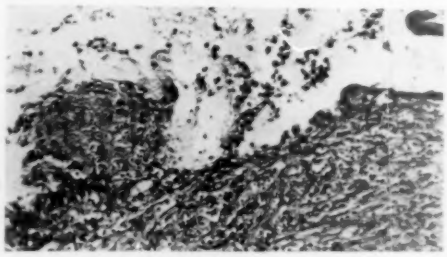

FIG. 7.—Isolated tuft or bud of granulation tissue in the base of a large ulcer near the margin of the lesion. Atypical epithelial cells are growing out from the ulcer edge (× 120).

TYPES OF HEALING

Two lesions were healed except for slight erosion of the epithelium covering the base of the ulcer. One of the patients, however, had multiple gastric ulcers (three), and two of the lesions were only partly healed. The

other patient had been on a liquid diet for approximately a year and during this time the symptoms, which had been present for forty years, had been partly relieved.

In seventeen cases epithelium grew from the margin of the ulcer; in seven granulation-tissue buds developed at the rim in the centre of the ulcer, but the lesions were not healed.

In twelve cases epithelium grew from the edge of the ulcer and granulation tissue was present in the base.

In four cases the only healing noted was manifested by epithelium growing from the margin of the ulcer and the organization of hemorrhage of the base.

In five cases evidence of healing was not found. Two of these ulcers were perforating. One patient was a physician who had been on medical management for two weeks without satisfactory results; acids had not been controlled. One patient was a nurse with an acute ulcer without fibrosis in the base. There were many polymorphonuclear leucocytes in abscess-like clumps. She had had multiple recurring gastric ulcers.

In two cases the ulcers were of the perforating type with marked arterial changes.

Although attempts were not made, except in one case, to treat the patients medically, a comparison of the healing changes found in the cases in which pre-operative preparation was given and in those in which it was not given revealed, as would be expected, practically the same state of healing. It is obvious that since the cases studied were not under observation with the idea of treating the lesions medically, but rather to relieve complications (chiefly gastric retention and dehydration) no great difference would be expected in the stages of healing. In experimental ulcers Mann has found that the average time required for healing after gastro-enterostomy or entero-enterostomy was about three weeks.

One of the gastric ulcers which was removed without previous treatment was completely covered by epithelium. Two had mushrooms of granulation tissue at the margin of the crater, epithelium at the edge and granulation tissue in the base. Two had epithelium at the margin and granulation tissue in the base; one had only epithelium growing out at the rim, and one showed no evidence of healing. This last ulcer was of the perforating type.

The size of the lesion was an important factor in healing. The larger and deeper the excavation the longer and more difficult the healing process. In many of the large lesions there were small scattered mushrooms of granulation tissue in the cavity as well as at the margin. (Figs. 7 and 8.) The granulation-tissue buds at the margin of the ulcer appear to be a method of defense of the organism against the marginal enlargement of the lesion. As the usual soft spongy granulation tissue in the base is gradually replaced by fibrosis due to the duration of the lesion and to trauma, the development of the granulation-tissue buds becomes more difficult and their survival more uncertain.

Gram-positive diplococci similar to those described by Rosenow,[35, 36] Gerdine and Helmholz, and others[8, 13, 19] were usually found in the deeper granulation tissue in the base of chronic ulcers and in no other place except on the surface of the adjacent mucosa. *Oidium albicans* was not found in the gastric ulcers in this series. Askanazy and Merke have found this organism frequently in gastric ulcers at operation and at necropsy.

FIG. 8.—Granulation tissue plug at the margin of a large ulcer with epithelium growing out as a single flat layer (× 40).

Fourteen of the thirty cases of gastric ulcer were apparently recurrent; that is, the ulceration was over an area of fibrosis in the wall which extended into the musculature beyond the marginal limits of the denuded area. The epithelium covering the affected areas was atypical as already described, and occasionally the well-known cystic deformed glands were present in the deeper layers of the mucosa. (Fig. 10.) All but one of the patients gave a history of intermittent distress suggestive of recurring ulceration or formation of a new ulcer.

According to Moore "partially healed gastric lesions give no signs in the röntgenogram that distinguish them from active ulcer. As long as there is any activity in the lesion (unhealed area), particularly in its centre, the Röntgen-ray reveals signs of a lesion."

DISCUSSION

In twenty-five of the thirty cases there were healing changes in the gastric lesions of one type or another. The five in which healing was not demonstrated were all of the perforating type and two of these were acute. In one of the two cases in which the lesions exhibited the most advanced healing there were multiple ulcers, one of which was almost completely covered by epithelium; the others were still ulcerated. In the other case the lesion was high on the lesser curvature of the stomach with an hour-glass deformity. The patient lived on liquid food for approximately a year. The lesion was almost completely covered by epithelium but some distress remained.

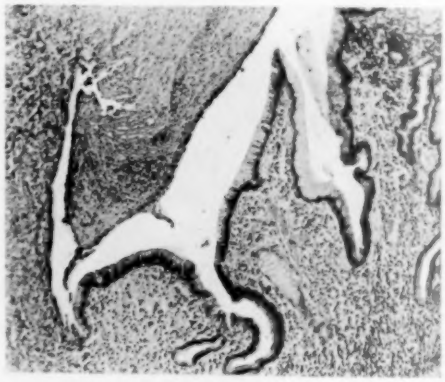

FIG. 9.—Higher magnification of the same field as that shown in Fig. 8 revealing the epithelium growing from the ulcer margin as a single row of cells.

The intermittent recurrence of symptoms in cases of peptic ulcer may be due to recurring ulceration, partial healing, or formation of a new ulcer. There are not, as far as we know, any definite criteria for judging at what

stage of healing symptoms disappear. Data obtained with a gastroscope are inconclusive since the stage of healing cannot be determined. The covering of the denuded area with epithelium does not necessarily indicate that the lesion ceases to cause symptoms. It is probable that the inflammatory reaction deep in the wall with the accompanying changes must subside in whole or in part before symptoms cease. The size of the lesion is an important factor in repair. If lesions are large the reparative processes are so retarded or are so ineffective that they cannot obtain their objective. Ulcers with overhanging borders which tend to protect the granulation-tissue plug in the base heal apparently much more rapidly than the larger lesions.[8, 10, 19, 33] The poor blood supply in the base of large lesions, the exposure of the reparative elements to traumatic agents, combined with hyperacidity, pylorospasm and the patient's lowered resistance, are a few of the elements that defeat the healing process. Perforating ulcers of the acute type with steep walls and punched-out appearance, and of the more chronic type (that is, developing in the base of an already established chronic ulcer) showed little or no healing. The marked vascular changes, endarteritis and thrombosis, so frequently found in the base of these lesions, suggest a possible reason for this peculiar behavior. The necrotic material must slough out before healthy granulation tissue becomes available for extensive repair. It seems likely that many ulcers start as small erosions which heal, recur, and break down, and the base enlarges, becomes more fibrotic, heals again and breaks down again. The fibrous tissue in the base continues to become more dense. The lesion with each recurrence enlarges concentrically and penetrates deep into the wall. Finally the ulcer becomes so large and fibrotic and the blood supply is so poor that granulation-tissue buds cannot form, or if formed, cannot persist, and so the keystone of the defensive and healing mechanism is lost. Although I have not seen a large ulcer healed by the formation or multiple buds of granulation-tissue in the base, the marginal encroachment of the lesion has doubtless been retarded by growth of the small granulation-tissue tufts. (Figs. 8 and 9.)

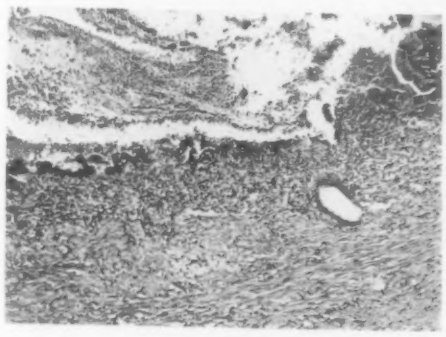

FIG. 10.—Erosion in the base of a recurring gastric ulcer. Cystic glands are shown in the fibrous connective tissue of the ulcer base.

SUMMARY

Healing changes were apparent in all except five of the thirty gastric ulcers in this series; these five were of the perforating type. The keystone of the healing factors was the granulation-tissue plug first described by Mann in experimentally produced peptic lesions. The size of the ulcer was a significant factor in healing. Large ulcers heal with much more difficulty

than small ones. In the former multiple granulation-tissue plugs may form in the crater or at the margin of the lesions; this latter probably is a defense against the marginal enlargement of the ulcer. Complete healing of a large ulcer by the formation of multiple buds of granulation-tissue was not observed. Epithelium at the margin of the lesions grew out as a single flat layer of cells and covered the granulation-tissue mushroom in the excavation. Later the connective tissue contracted and formed a scar-filled defect covered by atypical epithelium.

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INGUINAL ENDOMETRIOSIS

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The recent interest which has been aroused in ectopic endometrial tissue and the relative infrequency of inguinal endometriosis seems to warrant the placing on record of the following case:

Mrs. E. B., aged fifty, was first seen on June 2, 1927. At this time she complained of pain and tenderness in the right inguinal region at about the site of the external inguinal ring. She had been told by a physician, she said, that she had an inguinal hernia. At the external ring was a smooth rounded swelling which was exceedingly tender. Efforts at coughing were painful and no impulse could be felt at the ring. A tentative diagnosis of incarceration of omentum in an inguinal hernia was made and the patient was sent to a hospital. The white blood count was normal and there was no nausea or elevation of temperature. At operation the incision was made over the swelling and cautiously deepened. The empty sac of a small oblique inguinal hernia was entered. At the bottom of the sac, and a part of it, was a firm fibrous swelling some 5 x 4 x 4 cm. There were no sharp borders or capsules to this swelling which was intimately attached to, and a part of, the rectus sheath. The tissue was carefully dissected out, it being necessary to remove a portion of the rectus sheath. During the removal the dense mass was occasionally cut into and small cyst-like cavities were encountered. These were perhaps 0.5 cm. in diameter and contained a thick chocolate-like fluid. The inguinal hernia was repaired and the wound closed. A hæmatoma developed in the wound some days after the operation. This was evacuated and healed after packing. Otherwise her convalescence was uneventful and she was delighted that her pain was gone. She was discharged from the hospital on July 1, 1927.

The report of the pathologist on the excised tissue was as follows:

"A piece of indurated fibrous tissue and fat, 9 x 5.2 x 2.6 cm., cut surfaces of which are composed of firm gray-white tissue containing small areas of hemorrhage. In one portion there is a cyst 1.1 cm. in diameter filled with brown semi-solid material and having a slightly nodular lining (Sections).

"There are also two small pieces of indurated connective tissue and fat together equal to 2 c.cm.

"Microscopic: Sections of this tissue disclose fat with dense connective tissue containing small areas of ancient hemorrhage and patches of cellular infiltration with lymphocytes and endothelial leucocytes. There are a few small tubules in this tissue which resemble similar structures seen in the endometrium and these have patches of submucous hemorrhage and masses of granulation tissue attached.

"Diagnosis: Chronic inflammation; transplantation of the endometrium."

Further details of her history were obtained after the operation. She stated she first began to have the pain in the right inguinal region over fifteen years ago and was never entirely free of pain since, although there were variations in its intensity. The pain in the swelling was greater at the time of her menstrual periods and at these times the lump became larger. The menses were painful but regular and lasted five to six days. The hernia was first suspected twelve years ago. The patient had had four normal deliveries, three miscarriages, and no curettages (over a period of seven years). In 1918

she was told that removal of the uterus would help the pain and accordingly in February of that year, a supra-vaginal hysterectomy was done. Since that time, however, the pain has persisted and *was worse at the times when she should have had her menstrual period.*

Inguinal endometriosis has been defined as the presence of endometrial tissue in the groin. The first reported instance was Cullen's case.[1] Here "the growth" was removed and two years later a similar lesion was removed from opposite side. Since that time studies of Sampson [2, 3, 4, 5, 6, 7, 8, 9, 10] have added much to our knowledge of the subject.

Endometrial proliferations have been found on the intestines (rectum, sigmoid, lower mesentery, appendix) and Douglas' peritoneum (rectovaginal septum, posterior wall of uterus, tubes, uterine ligament, ovarian ligament, and bladder),[11] and in laparotomy scars. These proliferations correspond closely to the endometrium histologically and functionally. In 1925, Lemon and Manle[12] reported nine cases in women of ectopic adenomyomata derived from uterine mucosa which had invaded abdominal wall.

FIG. 1.—Photomicrograph of excised tissue. Note tubule lined with epithelium and areas of hemorrhage just outside of tubule.

The origin of these structures is still debated. By some they are regarded as derivatives of a cast-off embryonic portion of the Mullerian duct. Sampson's theory[2] that these proliferations are implantations of endometrium seems to be most reasonable and is supported by the excellent evidence obtained in his studies. Sampson believes that a retrograde menstrual flow which may be either spontaneous or incurred by instrumentation may cause bits of uterine mucosa or tubal epithelium to escape into the peritoneal cavity. These small bits of epithelium may implant themselves on any part of the adjacent peritoneum and there live and proliferate. They may grow upon the ovary and give rise to "chocolate cysts." They may, in any situation, react to menstruation and give off secondary implants. That uterine tissue may be transplanted to other parts of the body and grow has been

demonstrated.[13, 14] Jacobson [15] showed that bits of uterine mucosa scattered into the pelvic cavity of a monkey gave rise to peritoneal implants of this tissue. Sampson [10] calls attention to the fact that occasionally blood is observed escaping from the tubes of patients who are operated upon during their menstrual period, and notes that in 257 cases of peritoneal endometriosis both tubes were patent in 250 cases, one tube open in one, and in the six cases where there was occlusion of both tubes, the peritoneal lesion might have been present before the tubes were closed. It has been suggested that possibly uterine epithelium does not escape from the tubes but that the menstrual blood is capable of causing an endometrial metaplasia of the peritoneum with which it comes in contact.

In 1925, Sampson reported three cases of inguinal endometriosis.[8] In all three of these cases the nodule in the groin reacted to menstruation by becoming more tender at that time. In 1926, Sampson reported a case of "endometriosis of the sac of a right inguinal hernia, associated with a pelvic peritoneal endometriosis and an endometrial cyst of the ovary." [10] This patient, an unmarried woman of forty-four, complained of a right inguinal hernia. In the year previous to operation she was more conscious of her hernia during her menstrual periods. Sampson's pre-operative diagnosis was "right inguinal hernia, probably containing omental tissue." The peritoneum about the right internal abdominal ring was puckered and pigmented. The right round ligament, including the peritoneum about the internal abdominal ring and the entire hernial sac were removed in one piece.

The case reported in this paper is of unusual interest as the inguinal endometriosis might have been explained as a laparotomy implant following the hysterectomy were it not for the patient's unqualified statement that the painful nodule which reacted to menstruation antedated the hysterectomy. The existence of a right oblique inguinal hernia and the presence of the endometriosis at the bottom of the sac lend considerable weight to Sampson's implantation theory. It would seem that an endometrial implant, after being extruded from the tubes, had found its way into the hernial sac and had proliferated at the bottom of it. The hernia had probably never given any symptoms and in fact, was so small that it might possibly be termed a canal of Nuck, a circumstance, however, which does not vitiate the implantation theory in this case.

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TULAREMIA*

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The bacterium tularense was first isolated by McCoy and Chapin in 1912, in Tulare County, California, where the disease resulting from the inroads of this organism was discovered among ground squirrels.

Tularemia occurs in nature as a fatal bacteriæmia in ground squirrels, various species of wild rabbits and other rodents. It is transmitted to man, by the bite of the infected blood-sucking fly, tick, or bedbug, or by contamination of the hands, or conjunctival sac with portions of the internal organs, or body fluids of infected rodents or insects. Many cases occur in different parts of America during the rabbit hunting season, among those who dress or otherwise handle wild rabbits.

The disease has been reported from practically every state in the United States and from Japan. It has appeared in every month of the year, the seasonal incidence being in relationship to the seasonal prevalence of the insects which harbor the organism and also in relationship to the hunting season for rabbits in different localities.

Farmers and their families furnish the largest number of cases, because their occupation exposes them to flies, ticks and wild rabbits. Market men and women, housewives and cooks furnish a second group, and hunters and laboratory workers furnish a large third group.

Approximately 300 cases of tularemia have been reported, and in a study of a series of 220 cases by Francis [1] it was noted that 168 were males, and 52 were females, that the ages ranged from two to seventy-three years. Of this series, eight were negroes.

In most of the attacks occurring in man, the individual has become infected by dressing rabbits, performing necropsies on guinea pigs, rabbits, or white mice, or in handling living rabbits, guinea pigs and living ticks. Cases have been reported following the bite of a hog and of a coyote, and another after the bite of a ground squirrel. It is presumed that the mouth parts of these animals were contaminated by infected rabbits which they had eaten, because dead infected rabbits were found nearby.

* "The disease is named Tularemia on account of the presence in the blood of the causative organism Bacterium Tularense. This organism was so named by McCoy and Chapin who discovered it in 1912 as the cause of a fatal epidemic among the ground squirrels of Tulare County, California. Tulare County was so named because that region was once covered with extensive marshy beds of the reed tule, a large variety of bulrush." Francis, Edward, Second Ludvig Hektoen Lecture of the Billings Foundation, from the Proceedings of the Institute of Medicine, Chicago, 1926.

There is one record of transfer of the disease from man to man. This was the case reported by Harris,[2] in which a mother is believed to have contracted tularemia through accidently pricking her thumb, while changing the dressing of her son who was ill with the disease. No case has been reported of the spread of the infection from man to man by contact, nor by the bite of an insect. Surgeons who have incised or excised suppurating glands have not been known to contract the disease.

In a study of 110 cases Francis[1] found only 27 in which there was an abrasion which apparently was the avenue of infection. He found that the infection will pass through the normal guinea pig skin without abrasion, and without rubbing, but will cause a papule at the site of the infection. Cultures from human blood taken during the first week of illness indicate that there is a bacteriæmia early in the disease. In 77 cases the incubation period was found to be from twenty-four hours to nine days; the average being slightly more than three days.

In 220 cases, four clinical types of the disease were noted. They are: First, ulceroglandular, the primary lesion being a papule; later an ulcer of the skin, and accompanied by enlargement of the regional lymph-glands. Second, oculoglandular, the primary lesion being a conjunctivitis, accompanied by enlargement of the regional lymph-glands. Third, glandular, without primary lesion, but with enlargement of the regional lymph-glands. Fourth, typhoidal, without primary lesion, and without glandular enlargement. Fulminating cases running a rapid course with death, have been noted in the oculoglandular type.

The onset is sudden, and frequently occurs while the patient is at work. It is characterized by fever, headache, vomiting, chilliness, general aching, sweating and prostration. Fever, sweating and prostration persist generally three to four weeks, the fever being intermittent.

In the ulceroglandular type, the patient complains, within forty-eight hours after the onset, of pain in the area of the lymph-glands, which drain the site of the infection. These glandular pains may precede any reference by the patient to the site of infection, which is a swollen, inflamed papule. This breaks down after a few days, liberating a necrotic core or plug, and leaving an ulcer often about three-eighths of an inch (1 cm.) in diameter, with raised edges and having a punched-out appearance. On healing, the ulcer is replaced by scar tissue. The skin is often red over the enlarged and tender lymph-glands, and red streaks may be visible along the lymphatics of the extremity. In about half of the cases, the lymph-glands proceed to suppuration, and if not incised, may rupture through the skin. In other cases, the glands do not break down, but remain hard, palpable, and rather tender for two or three months, gradually returning to normal. Lymph-glands other than the regional glands are usually also affected. Subcutaneous nodules simulating sporotrichosis will usually be present along the course of the lymphatics. These nodules as a rule are distributed over the posterior surface of the forearm and arm, between the ulcer and the enlarged axillary glands.

They are firm and movable, about .5 cm. in diameter and number from 5 to 50 in each case.

The oculoglandular type follows the general description of the ulceroglandular, the primary localization being in the conjunctival sac instead of the skin. Of 15 cases reported, 12 were unilateral, and three were bilateral. In the early stage, there is irritation and lacrimation of the eyes, swelling of the lids and surrounding tissues, œdema of the conjunctiva, and usually a papule on the conjunctiva of the lower lid. At the same time there are swelling, tenderness and pain in the surrounding lymphglands, which in severe cases extends to the cervical and axillary group. Small, discrete ulcers appear very soon on the conjunctiva of both lids. A purulent dacryocystitis has been noted in two cases. No involvement of sinuses has been found. Permanent impairment of vision occurred in one case, which proceeded to blindness following a perforation of the cornea and resulted in fusion of the cornea and iris into a compact mass. The constitutional reaction is manifest by fever, chills, sweating, prostration, and in severe cases, by convulsions.

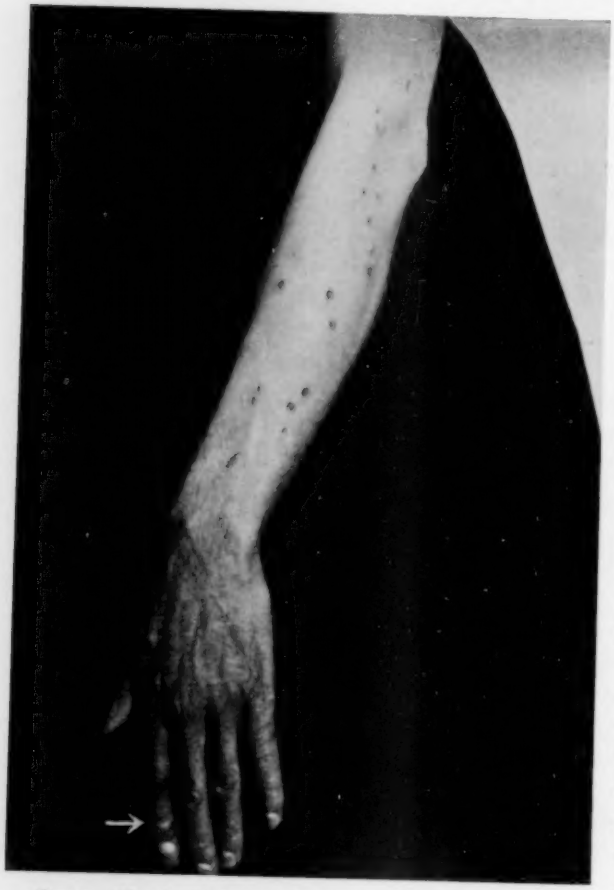

FIG. 1.—Showing lesions of forearm and hand (subcutaneous nodules), some of which have been punctured and pus evacuated. Arrow points to site of initial lesion on index finger.

In the glandular type the clinical picture is generally that of the ulceroglandular form with the exception that no primary lesion is evident. In the typhoidal type, fever is the outstanding symptom, the onset and duration being similar to that of the glandular type. Diagnosis is confirmed by a positive agglutination test and a negative widal.

Tularemia has been erroneously diagnosed influenza, septic infection, typhoid fever and sporotrichosis. Serologists have considered it undulant fever on account of the cross agglutination of Melitensis and Abortus.

Pathologists have described the lesions in the lymph-glands as tuberculous. In laboratory workers suffering with the typhoidal type, a history of having worked with, or near animals or insects infected with the disease, is given.

Aside from laboratory workers, patients usually give a history of having dressed wild rabbit, or having been tick bitten, or fly bitten, and about three days later having experienced a sudden attack resembling in many respects an influenzial onset. This is followed by symptoms of local septicemia. The primary skin lesion first appears in the form of a papule, or there may be primary conjunctivitis. Early, persistent, glandular enlargement occurs in the region draining the primary lesion. Fever is always present at the onset of an initial attack. It is characterized by rise and remission lasting for several days, after which there is gradual decline to normal, lasting from one to three weeks. The diagnosis is confirmed by agglutination of the bacterium by the patient's blood serum. The blood is collected and forwarded as for a Wassermann test.† This test becomes positive during the second week of illness. Microscopic or cover glass preparations and cultures taken direct from the patient are considered useless. Guinea pig, or rabbit inoculations are best to determine the presence of the organisms.

FIG. 2.—Enlarged cervical gland at fourth week.

CASE REPORT.—W. E. S., a white man, aged thirty-two, American, married, on November 18, 1926, dressed several wild rabbits which he had shot in central Ohio. Forty-eight hours later he experienced chilly sensations while at work in his office, and later had a distinct rigor, followed soon by a temperature of 104.5 degrees. He was under the impression that he might be suffering from influenza. He had noticed

† In the absence of a convenient laboratory equipped for the diagnosis of tularemia by agglutination, blood specimens are best forwarded direct to the Hygienic Laboratory, Washington, D. C.

some discomfort in the right epitrochlear and axillary regions, and a small lesion upon the index finger.

Physical examination after the chill revealed a single round lesion on the flexor surface of the right index finger just over the distal joint. It was about .5 cm. in diameter and appeared as a dried bleb with a peculiar darkened centre and markedly red border.

Red lines along the course of the superficial lymphatics of the forearm were apparent, and the epitrochlear and axillary lymph-nodes seemed moderately swollen.

FIG. 3.—Incisions at site of epitrochlear and axillary abscesses.

Soon after the onset there was a peculiar, painful, involuntary twitching of the muscles of the right side of the face. After about thirty-six hours this symptom disappeared.

For two days after the onset, his temperature ranged from 103.5 degrees in the evenings, down to 100 in the mornings, and gradually subsided to about 101 in the evenings. About the tenth day the temperature again rose to 102 in the evenings. The pulse rate remained low or near normal; the volume rather full, somewhat similar generally to the pulse of typhoid fever. There was a slight intermittent epistaxis at first for two or three days. The chest and abdomen were negative. Nausea or vomiting did not occur. The leucocyte count at this time was 22,500. The blood Wassermann was negative. The urine showed a trace of albumen.

On the fifteenth day the epitrochlear glands seemed to fluctuate. He was admitted to the hospital and the epitrochlear region freely incised, evacuating about 10 c.c. of yellowish, odorless pus. The initial lesion on the index finger was excised. It had become an undermining ulcer with a small necrotic centre, and had shown no tendency to heal.

During the second week there appeared about two dozen other small lesions upon the effected hand and forearm. These developed as subcutaneous nodules along the course of the superficial lymphatic channels on the extensor surface of the hand and forearm. They were about .5 cm. or less in diameter, round, elevated and on palpation felt markedly indurated as though each might contain a bird shot. Nearly all were incised and a drop of thickened pus evacuated. There was one enlarged submaxillary gland on the right side, about 1.5 cm. in diameter.

The patient left the hospital on the twenty-eighth day with temperature normal except a fraction of a degree of fever in the evenings. On the thirty-fourth day there was again fever of 101 degrees. Two more infected epitrochlear glands which had appeared, were opened at this time, and free pus evacuated.

On the forty-first day, fluctuation appeared in the enlarged axillary glands. They were incised and about 15 c.c. of pus evacuated. Discharge never persisted after evacuation of affected areas, and on each occasion after incision, there was distinct improve-

ment generally, which lasted from five to seven days. During the fifth week there was only a fraction of a degree of fever, appearing usually at three or four-day intervals.

The patient began rapidly regaining his appetite and strength, and returned to part time professional duties about the seventh week. All lesions were healed by this time, leaving reddened scars. The lesions were never more than mildly painful. Weakness and exhaustion were marked, gradually disappearing during the fifth and sixth weeks Considerable weight was lost. The spleen did not enlarge to an appreciable degree, nor was there a general adenopathy or conjunctivitis during the attack. Pus from evacuated areas, during the third week, was reported positive for staphylococcus three times, and no growth on two occasions.

Blood serum sent to the Hygienic Laboratory at Washington, D. C., during the fifth week was immediately found strongly positive for tularemia, agglutinating the bacterium in dilutions up to one in 1280. Pus from the axillary region injected into a guinea pig at the Springfield Lake Sanatorium by Dr. C. L. Hyde, caused death in about four days, with changes in the spleen and liver typical of tularemia.

One attack confers immunity in man, which lasts at least for several months. It has been shown that the agglutinins in the blood of recovered patients persist over long periods of time, which may be an indication of immunity. Susceptible laboratory animals have exhibited no evidence of acquired immunity. Thorough cooking is found to render meat harmless as food. Laboratory workers engaged in performing necropsies usually wear rubber gloves and follow careful technic. Cooks, market men and hunters should wear rubber gloves in dressing rabbits. Treatment is largely symptomatic. Rest in bed is of course imperative. Excision and drainage of broken down glands causes a remission of temperature and immediate general improvement. No prophylactic or curative serologic product has been perfected.

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THE CLINICAL MANIFESTATIONS OF NON-METALLIC PERFORATING INTESTINAL FOREIGN BODIES

By Leon Ginzburg, M.D.

AND

A. J. Beller, M.D.

of New York, N. Y.

FROM THE SURGICAL SERVICES OF THE MOUNT SINAI HOSPITAL

The occasions on which foreign bodies, such as chicken or fish bones are accidentally swallowed with the food, must be very numerous. Usually unless they lodge in the pharynx or œsophagus, they give rise to no immediate symptoms or alarm, and doubtlessly in the great number of instances, are passed without further incident. In certain cases, however, the relative frequency of which it is obviously impossible to determine, their further progress becomes arrested at some point in the intestinal tract. Then, as a result of their physical characteristics which conduce to penetration and perforation, they may give rise to clinical manifestations which are extremely puzzling.

A word of explanation is perhaps in order to account for the limitation of this communication to the consideration of only *non-metallic* foreign bodies. Metallic foreign bodies are excluded because they present a different clinical problem. The ingestion of one of these objects, such as a pin, needle, etc., is a more or less dramatic and alarming event, which brings the patient under observation at once, or at least impresses itself vividly upon his memory. The problem then resolves itself into the observation and treatment of a potentially perforating foreign body, known to be present in the gastro-enteric tract. Furthermore the ease with which they are demonstrated by the X-ray, gives definite knowledge of their presence, and facilitates the subsequent study of their course. With the non-metallic type of foreign body, under discussion, however, the patient presents himself as a rule only after perforation has occurred. And, as will be seen, with marked variations in the clinical picture. By this time, he has forgotten, if he ever noted, the swallowing of a chicken or fish bone, and he certainly never thinks of connecting the present serious plight, with so minor an occurrence. The X-ray of these cases is of practically no assistance.

In the twelve cases, which are here reported, fish bones were found six times, fragments of chicken bone five times, and a sliver of wood (tooth-pick) once. However, any relatively short, sharp-pointed non-metallic foreign body, would fall into this category. In the literature, cases due to bristle, bits of stubble, a piece of cherry stem, etc., have been reported. Fish bones, however, are by far the most frequent.

The cæcum and flexures of the colon are the most frequent sites of perforation. Arrest of one of these foreign bodies in the normal small intestine, is uncommon. On the other hand, conditions such as prevail in a large hernial sac, tend to favor the lodging of a sharp-pointed object at that point.

The presence of a Meckel's diverticulum is an increased hazard. A few scattered cases of perforation of the stomach and duodenum have been reported. Rectal perforation is very common, and gives rise to symptoms of proctitis, ischio-rectal abscess, and fistula. They are, however, outside of the scope of this paper, which is limited to cases occurring intra-abdominally.

The first effect of the arrest of the foreign body is an abrasion of the mucosa with the formation of a small ulcer. A continuation of the pressure, results in an area of necrosis, progressively involving the different layers of the intestinal wall. Through this breech, intestinal organisms pass, giving rise to a local peritonitic reaction, even before actual perforation has occurred. Some of the cases of peri-colitis and omentitis, of undetermined origin, may very well be due to foreign bodies, which, having produced this degree of injury, dropped back into the intestinal lumen, and are passed per vias naturalis.

When actual perforation does occur, the response varies with its rate. If rapid, a diffuse peritoneal exudate or localized abscess results. The slowly perforating types, on the other hand, incite a reaction which is mainly productive, an inflammatory granulation tissue resulting, which may contain pin-point abscesses. If the foreign body is removed, these masses usually undergo complete resolution. The continued presence of a foreign body, however, prevents the complete subsidence of the infection, and finally leads to the production of a dense fibrotic tissue with scattered foci of acute inflammation. Multinuclear giant cells are usually found in the immediate vicinity of the foreign body.

Erosions of the blood-vessels are rare. Arling [1] reports a case of fatal gastric hemorrhage in a sixty-six year old man, which at autopsy, was found to be due to a fish bone perforating the posterior gastric wall. When the perforation occurs along the mesenteric border of the bowel, there is a possibility of a purulent thrombophlebitis. Benda [2] reports such a case in which a fish bone was found in the superior mesenteric vein, the ileo-colic branch of which was thrombosed. Wettergren [3] reports a case of multiple pylephlebitic liver abscesses, in one of which a fish bone was found. While involvement of these larger vessels is rare, it is probable that the slow pressure necrosis incident to perforation produces a certain degree of thrombophlebitis in the small intramural intestinal radicals, a fact, which would serve to explain the rather frequent history of chills in both our own and in the reported cases.

Omitting from consideration the rather rare and bizarre manifestations which may be caused by the migration of the foreign body, the cases encountered by the surgeon fall into the following groups:

1. Acute peritonitis.
2. Localized intra-abdominal abscess.
3. Intra-abdominal inflammatory tumors.
4. Inflammatory tumors of the abdominal wall.
5. Abscess of the abdominal wall.
6. Inflammation and obstruction in a hernial sac.

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TYPE I.—*Cases with Symptoms of Peritonitis.*—These are relatively uncommon, and are caused by foreign bodies which become impacted when lying transversely to the long axis of the bowel. Chicken bones are apparently the most frequent cause, and the lower ileum, the narrowest portion of the small intestine, the most common site of this type of perforation. Three different mechanisms are possible.

(a) The foreign body produces an area of necrosis, and gradually works its way through. In this type there are apt to be two areas of necrosis, namely one at each end of the foreign body. (Case I.)

(b) An area of necrosis results. The foreign body may pass on, but secondary perforation occurs due to a sloughing of the compromised area.

(c) A foreign body of small diameter, and very sharp and rigid, may be pushed through the intestinal wall, with the production of a minimum amount of necrosis. In this type of case there may be perforation into an adjacent viscus.

The onset of symptoms in these cases is fairly sudden. The violent pain and shock ordinarily associated with perforation of a hollow viscus is absent. This is probably due to the fact that as these perforations occur rather slowly, a certain degree of peritoneal reaction ensues, before actual perforation takes place. Furthermore, the foreign body may act as a plug, thus preventing the escape of large quantities of intestinal contents. The usual signs and symptoms of peritonitis are present, but are too indefinite to give any clue as to its point of origin. The diagnosis of appendicitis is usually made. Upon laparotomy a sero-purulent exudate is found, there being no evidence of gross intestinal soiling. The usual foci are found to be normal, and further exploration reveals the presence of a foreign body. Its location is facilitated by the fact that there is a certain degree of dilatation above and constriction below it.

CASE I.—S. B., age fifty-three, was admitted to the Mt. Sinai Hospital, November 7, 1924, with a history of having had recurrent generalized abdominal colic at intervals, for the past few weeks. Three days ago, the pain became much more severe, and tended to localize in the right lower quadrant. On the day before admission, he had had a chill, was nauseated, and vomited. His temperature was 101° F. Examination of the abdomen revealed moderate distention with direct and rebound tenderness equal in both lower quadrants. No masses palpable. Rectal examination negative. A tentative diagnosis of appendicitis with peritonitis was made. At operation, the abdomen was opened through a right rectus incision. A considerable quantity of sero-sanguinous fluid escaped. The intestines were covered with scattered areas of fibrin. Exploration of the appendix, gall-bladder and colon, revealed no abnormalities. On further examination, a greatly dilated and congested loop of ileum was encountered. Immediately below it the gut was slightly collapsed. Closer inspection revealed an area of necrosis, about 2 cm. in diameter, with a small perforation at its centre. This was due to a chicken bone, 2 inches in length, lying transversely in the bowel. There was no perforation on the opposite side of impingement. The chicken bone was removed, and the necrotic area, together with the perforation, inverted by two rows of Lembert sutures. Because of the friable nature of the intestine, and its narrowing by the inverted sutures, a short-circuiting entero-anastomosis was deemed advisable. After a rather stormy convalescence, patient made a complete recovery.

The next case, while not proven, and not one of our 12 cases, is reported as a possible illustration of secondary perforation due to foreign body.

Case II.—B. K., nineteen years of age, was admitted to Mt. Sinai Hospital, September 18, 1919. Six hours prior to his admission, he had suddenly developed very severe lower abdominal pain, stabbing in character, and more marked on the right side. He was nauseated, but did not vomit. On admission, his temperature was 102° F. Examination revealed an acutely ill young man, with an extremely rigid and tender lower abdomen. Immediate laparotomy was performed through a right rectus incision. There was an escape of free sero-purulent fluid. The appendix was normal. Further exploration revealed the fragment of necrotic tissue attached to the bladder, near which a loop of small intestine was found, which was markedly infected. At a short distance from this point, a perforation one-half to one cm. in diameter was encountered. The perforation was closed in two layers, and the fragment of necrotic tissue previously mentioned, excised for pathological examination. This specimen was reported as a "thin fibrous layer, partially covered with epithelium, and containing multinuclear giant cells." The peritonitis progressed, and the patient died. Post-mortem examination revealed a competent enterorrhaphy, and bronchopneumonia. A thorough study of the intestine showed no other evidence of any pathological lesion, nor could any foreign body be found. The most probable explanation in this case, in view of the presence of multinuclear giant cells in the fragments of necrotic tissue, which had evidently formed the base of the ulcer, is as follows: A foreign body probably became arrested in the small intestine, causing an area of necrosis, which was sealed off by adhesions to the bladder. This area secondarily sloughed out, giving rise to an intestinal perforation.

Type II.—*Cases with Localized Intra-abdominal Abscesses.*—These are probably the most frequent clinical manifestations of non-metallic perforative foreign bodies. A fairly large number of cases appear in the literature. They are usually the result of penetration of the large intestine, the greater frequency at this site being due to the sacculation, haustration, and relative thinness of the colonic wall. When occurring in the cæcum, they are usually diagnosed as appendicular abscesses. At the hepatic flexure they are mistaken for peri-cholecystic abscesses, or abscesses due to an unusually high appendix. The differentiation from a perforated carcinoma of the colon or diverticulitis frequently comes up. When peri-colonic abscesses are opened, the escaping pus should be carefully observed. If a foreign body is present, it usually is floated out. At times, however, the foreign body may be found in an omental abscess. When the foreign body is found, no attempt should be made to locate the site of perforation, as this type usually closes spontaneously. No fecal fistulæ have been observed in our cases after simple drainage. In one case the colon was examined with a barium enema about ten days after the incision of a foreign body peri-colonic abscess. No evidence of any communication between the colon and the abscess cavity was visualized.

The pus is usually very foul. Tube or rubber dam drainage with ample provision for drainage of the superficial layers of the wound leads to closure within a few weeks.

Case III.—R. P., was admitted to Mt. Sinai Hospital, January 31, 1925, with a history of having been ill for five days. There was loss of appetite, nausea, and severe epigastric and right upper quadrant pain. He claimed that he had had a similar attack one year ago. On admission, temperature was 102° F. There were some vague signs

at the base of the right lung. The upper abdomen was rigid throughout. Tenderness, both direct and rebound, was most marked in the right upper quadrant. The white count was 8500 with 80 per cent. polymorphonuclears. The case was considered to be either a peri-cholecystic abscess or a slowly perforating duodenal ulcer, which was being walled off. Under observation the upper abdominal rigidity and tenderness localized definitely to the right upper quadrant. The white blood count rose gradually to 19,000, and finally a distinct mass could be palpated in the right upper abdomen. A diagnosis of pericholecystitic abscess was made, and the abdomen opened through an upper right rectus incision. An abscess cavity containing large quantities of foul-smelling pus was entered. As the pus escaped, a fishbone, about one inch in length, was detected. The abscess cavity was sponged dry, and a small sinus was found leading downward and to the right toward the hepatic flexure. A tube was passed down to the sinus, and the abdomen closed in layers. There was profuse drainage and fascial necrosis occurred. The wound was opened down to the fascia, and allowed to heal by granulation. There was complete healing within a few weeks, without fecal discharge occurring at any time. It was interesting to note that bacterial culture of the pus showed no evidence of colon bacilli, only an anhæmolytic streptococcus being found. Unfortunately, no direct smears or anaërobic studies were made, but it is probable that anaërobic intestinal organisms were present in addition to the streptococcus, and accounted for the foul odor of the pus.

Case IV.—J. D., age forty, was admitted to the Mt. Sinai Hospital, August 18, 1920. Five days before admission, the patient noted marked abdominal distention upon awakening. Shortly afterward he vomited. Two days later there followed pain in the right lower quadrant, which has persisted to date. Temperature was 101° F. Abdominal examination revealed a slightly tender mass about the size of a small orange, in the right lower quadrant. Rectal examination was negative. A pre-operative diagnosis of appendicitis with abscess was made, and the abdomen opened through a four-inch Kammerer incision. The appendix was delivered, and found to be normal. On further examination, a retrocolic mass was palpated. The peritoneum alongside the colon was incised, and the latter mobilized. A small retrocolic abscess was discovered, and evacuated. In the posterior wall of the upper part of the cæcum, a fragment of toothpick, about one inch in length, was discovered, lying apparently completely outside of the lumen. Near this the cæcal wall was necrotic for an area about 1 cm. in diameter. The toothpick was removed, and the necrotic area sutured over. The retrocæcal region was drained with a rubber tube, and the patient made an uneventful recovery. The interesting point about this case is that the abscess was really retroperitoneal, and if operation had been delayed, might have pointed as a lumbar abscess.

Case V.—E. B., age twenty-seven, was admitted to Mt. Sinai Hospital, October 20, 1917, with a history of pain in the left hypochondrium of two months' duration. He had had three such attacks, each one lasting about five days. The present attack had begun four or five days before admission. The temperature was 102° F. Examination revealed a tender mass in the left upper quadrant of the abdomen, apparently an intra-abdominal abscess. White blood count was 17,000 with 77 per cent. polymorphonuclear. At operation, the abdomen was opened through a left upper rectus muscle splitting incision. The posterior rectus sheath and peritoneum were thickened and œdematous. Adherent to the peritoneum was a walled-off abscess. This was opened, and a large quantity of foul pus escaped in the course of which a fish bone was found. The abscess cavity was drained with a rubber tube, and the perineal wound closed. The parietal wound was partly closed, and the portion around the tube packed lightly with gauze. There was a rapid, uneventful recovery.

Case VI.—R. B., age forty-seven, was admitted to the Mt. Sinai Hospital, with a history of severe pain in the left upper quadrant of a few weeks' duration. He had no other gastro-intestinal or any other symptoms. On admission, his temperature was 100.2° F. Physical examination disclosed a moderately tender mass in the left upper

quadrant. A perforating neoplasm of the colon was suspected, but a barium enema showed no abnormalities. Operation: The patient was explored through a six-inch upper left rectus incision. Beneath the rectus muscle, a small sinus was encountered, which led down to an abscess cavity encapsulated between a mass of omentum, and the anterior abdominal wall. The abscess was evacuated, and exploration of the omentum disclosed a small intra-omental abscess in which lay a fishbone. The omentum was seen to lie just anterior to the distal extremity of the transverse colon. Drainage: With a rubber tube, and closure of the abdomen in layers. The patient made an uneventful recovery.

TYPE III.—*Cases Presenting Themselves as Intra-abdominal Tumors.*—A few cases have been reported in the literature where the perforated foreign body was found after a portion of the colon had been resected; for what was apparently considered a malignant tumor. In a few other cases of resection for inflammatory peri-colonic tumors, where no foreign body was found, the descriptions of the operative findings are such, that one is led to suspect that a foreign body had been present, and perhaps later passed per vias naturalis, or migrated as in one of our cases. The three cases recorded below, all of whom were private patients of Dr. A. A. Berg, are to our belief the only ones reported in the literature in which the cause of the inflammatory peri-colonic tumor was suspected and the offending foreign bodies sought and found at operation. One of us (L. G.) was present at the operation in two of these cases, and Doctor Berg has been kind enough to furnish a description of the operative findings in the third.

This group is an extremely important one because of the mistakes that may be made in diagnosis, prognosis, and operative indications. The site of perforation is usually the colon, and takes place so slowly that acute symptoms are frequently lacking. A low grade infection results, in which the inflammatory reaction is mainly productive. In addition, there is a typical tissue reaction to the presence of a foreign body, such as described above. As a result, inflammatory peri-colonic masses of considerable size may be formed. In some cases the omentum becomes adherent, and secondarily involved with the formation of an inflammatory omental tumor. The foreign body may pass into the omentum, so that a mass of inflammatory granulation tissue remains around the colon, the etiology of which is in doubt even during the operation, because of the migration of the original causative factor. It must be emphasized that this type of inflammatory tumor is completely extra-colonic. They are not to be confused pathologically with other inflammatory granulomata of the bowel, such as reviewed by Tietze,[4] in Germany, and recently by Wilensky [5] and Moschcowitz in this country. In these, the mucosa and submucosa are the seat of ulcerative and chronic and subacute inflammatory changes. In the inflammatory tumors, which result from perforated foreign bodies, the mucous membrane, and the walls of the intestine, are not the seat of any marked changes, except perhaps for a small sinus, leading to the mass, lined perhaps with giant cells. At times, a slight scar is all that will mark the site of penetration.

The history in these cases is that of gradually increasing local pain and

tenderness, with the development of a large hard mass, which is frequently first noted by the patient himself. As there is no involvement of the gut proper, there are as a rule, no signs of obstruction or colitis. The severe colicky abdominal pain, characteristic of colonic neoplasm, is usually absent. Vomiting, diarrhœa and melena are infrequent. The disparity between the size of the mass, and the absence of impairment of nutrition, or anæmia, is striking. Röntgenologically there is no filling defect.

At operation, as pre-operatively, the main difficulty is to be sure that one is not dealing with carcinoma of the colon, for in the latter case a radical, and in the former, a conservative procedure is indicated. Differentiation from peri-diverticulitis may come up, but is of lesser importance. Some information may be gained from the inflammatory thickening of the posterior rectus sheath, and peritoneum, due to the long-standing infection, which is more common here than a carcinoma of the colon. These tumors are firm, but smooth, and do not encroach upon the intestinal lumen. Malignant tumors of the colon, on the other hand, are nodular, irregular, and can be felt to cause either stricture or irregular projections into the lumen of the gut. Small abscesses may at times be found in the inflammatory tumors, which should be carefully inspected after evacuation, as they may lead to the foreign body. The major portion of the inflammatory tumor may at times be formed chiefly by a mass of inflamed omentum.

Case VII.—A. K., was admitted to the Mount Sinai Hospital, July 20, 1926, with a complaint of pain in the left upper quadrant of the abdomen of eight weeks' duration. Pain was localized, and did not radiate. It was more or less constant, and had no definite relation to the intake of food. For the last three weeks, the bowels have moved only with the aid of cathartics. The patient also stated that the stools had become smaller in diameter. There was no melena, vomiting or diarrhœa, nor were there any urinary symptoms. He had lost 20 pounds in weight since the onset of his illness. However, he appeared to be fairly well nourished, and his hæmoglobin was 95 per cent. In the left upper quadrant of the abdomen, and in the left flank, a large, slightly tender mass, was palpable. In order to rule out the possibility of the mass being renal in origin, an X-ray of the urinary tract was taken. This showed the kidney to be normal in size and in position. X-ray of the colon showed no filling defect. A pre-operative diagnosis of inflammatory tumor, or carcinoma of the splenic flexure, was made. At operation, a large mass was found occupying the splenic flexure, and upper portion of the descending colon. This was carefully separated into two component parts, one of which consisted of thickened, inflamed omentum, the other was a large, smooth, firm, peri-colonic mass. There was no evidence of any invasion of the colonic lumen. In the midst of this mass there was seen to be a depressed area, of what was apparently a healed fistulous communication with the gut. The omental mass was then further explored, and two fish bones were found lying in separate small abscess cavities. The abdomen was closed with rubber tube drainage, and the patient made an uneventful recovery.

Case VIII.—Mrs. H., was admitted to Mt. Sinai Hospital, January 7, 1924. She had been previously operated on for chronic cholecystitis and cholelithiasis, and a cholecystectomy was performed. Following this, she was well for a few months, until a few weeks before admission, when she again developed severe pain in the right hypochondrium. This pain was continuous, and did not radiate. There was no jaundice. Concomitantly, the patient noticed the development of a tender mass in the right upper

quadrant. She gave a history of having had attacks of chills and fever, but during her stay at the hospital, her temperature remained normal. In the right upper quadrant of the abdomen, a large, hard, tender mass was palpable behind the old scar. The mass was only slightly tender. A pre-operative diagnosis of abscess, around the stump of the cystic duct was made. At operation, the incision was carried down through the old gall-bladder scar, which was excised. The posterior rectus sheath and peritoneum were greatly indurated, and œdematous, but showed no infiltration. A large mass was found occupying the region of the hepatic flexure of the colon. It was at first thought to be carcinoma, and the hepatic flexure was mobilized in order to permit of better inspection. The mass was found to be hard, but not nodular, and was apparently completely pericolonic, there being no invasion of the intestinal lumen. It was concluded that the mass was inflammatory in nature, and on further exploration, a fish bone, 2 to 3 cm. long, was discovered lying in inflammatory tissue. There was no evidence of the site of perforation, which had apparently healed over. There were a few drops of pus in various portions of this inflammatory tumor. The abdomen was closed with rubber tube drain, and an uneventful recovery ensued.

Case IX.—Mrs. R. V., was submitted to Mt. Sinai Hospital, June 29, 1926. She had been completely studied on the outside, and was sent for operation with a diagnosis of carcinoma of the colon. Unfortunately, the pre-operative findings are not at our disposal. On examination, a large, hard mass, slightly tender, was palpable in the right upper quadrant. Operation was undertaken for a suspected tumor of the hepatic flexure. As the peritoneum was opened, a small abscess was encountered, encapsulated between the anterior parietal peritoneum, and a large mass in the region of the hepatic flexure of the colon. The tumor gave the impression of being inflammatory in nature, and after a careful dissection a chicken-bone, about one-eighth of an inch in diameter, and two inches in length, was encountered, just protruding through the mass. Drainage with a rubber tube. After prolonged and profuse discharge of pus, patient was discharged from the hospital completely well.

Type IV.—*Cases Presenting Themselves as Tumors of the Abdominal Wall.*—These apparently develop a considerable time after the perforation of a foreign body. The symptoms following the original extrusion may be so mild as to occasion only slight disability, or as in our case to completely escape notice. The tumors are hard, fixed, and well demarcated. There may be no signs of inflammation. Desmoid of the abdominal wall, sarcoma, actinomycosis, and in smaller tumors, metastatic carcinoma, are usually considered in a differential diagnosis. The following should make one suspicious of an apparent abdominal wall tumor being due to a perforating foreign body.

(1) Its proximity to the umbilicus. (2) Its situation deep to the rectus muscle, to which it is frequently very adherent. (3) If on biopsy small collections of pus are encountered. In cases of doubt, of course, biopsy with microscopic examination should be performed.

Case X.—J. C., age sixty-five, was admitted to Mount Sinai Hospital, April 30, 1925. For the past few months the patient had noted the development of a mass above and to the right of the umbilicus. There had been no pain associated with its development. It had never been reducible. Physical examination showed a hard, smooth, spherical mass, about three inches in diameter, to the right and above the umbilicus. It was not tender, and there were no signs of inflammation. There was no cough impulse. The pre-operative diagnosis was that of a tumor of the abdominal wall, or an umbilical hernia, with irreducible, thickened omentum. An elliptical incision was made around the mass, and the tissues found to be normal down to the rectus muscle. The posterior

aspect of the rectus muscle, the posterior rectus sheath and peritoneum were involved in a mass of dense, grayish tissue. To effect its removal, the abdominal cavity had to be entered. The omentum was then found to be adherent to the mass, but was not apparently involved in the inflammatory process. There were no evidences of any adhesions of any of the abdominal viscera to the deep surface of the tumor. The tumor, when excised, was still considered to be a neoplasm, and the specimen was cut across for further inspection. In the depths of the mass a small collection of pus was found, and in its centre was a fish bone 2 to 3 cm. long. Culture showed staphylococcus albus, and an anhæmolytic streptococcus. The pathological description follows: "The macroscopic specimen consists of tumor mass, to which is attached a resected portion of omentum, and some adherent muscle. The tumor mass measures about 7 to 8 cm. in diameter, is oval in shape, firm in consistency, and on section presents a small sinus tract containing a foreign body about 3 cm. long. (Fish bone.) Microscopic examination discloses a fibroma showing numerous inflammatory areas. A few multinuclear giant cells are present in the tissue adjacent to the foreign body."

A practically similar case was found accidentally in the course of a general physical examination, is reported by Morian.[6] Stetten[7] recently presented a case before the New York Surgical Society, in which a small tumor in the region of the umbilicus, was removed under the suspicion that it might be a metastatic carcinomatous nodule. Upon excision, the tumor was found to consist of a central core, composed of a fish bone surrounded by thick, inspissated pus. Wölfler and Lieblein quote a case, where the suspicion of abdominal wall sarcoma existed. Biopsy was performed, and revealed a chronic inflammatory tissue. The mass was then thought to be actinomycosis. About six weeks later, there was a sudden discharge of pus, in which a cherry stem was found.

Type V.—*Cases Presenting Themselves as Abdominal Wall Abscesses.*—These result when the involved gut becomes adherent to the parietal peritoneum, before perforation occurs. The site of perforation closes very rapidly as a rule, so that an abscess containing intestinal bacteria may be found without any evident communication with the gut. If the foreign body is not discovered, when the abscess is opened, a chronically discharging sinus will, of course, develop.

Case XI.—T. H., age sixty-six, was admitted to Mount Sinai Hospital, in January, 1924, with a large red, painful swelling, occupying the antero-lateral aspect of the lower portion of the left chest, and extending down to the left upper quadrant. It had first appeared five weeks ago, and increased rapidly, in size since then. She had lost twenty pounds in weight, and felt weak, but there were no gastro-intestinal respiratory, or urinary symptoms.

Aspiration of the mass revealed pus from which Gram-negative bacilli (colon), and Gram-positive cocci and bacilli, were isolated. A perforating neoplasm of the splenic flexure was suspected, but a barium enema showed no abnormality of the colon. The abscess was laid wide open, and explored, but no communication with the gut could be found. Six months later she was re-admitted to the hospital with a sinus running downward and inward from its external opening at the ninth rib in the anterior axillary line. Injection of dyestuffs, and Röntgen examination, after the injection of opaque substances, failed to show any communication with the gastro-intestinal or genito-urinary tracts, or chest. There was no evidence of osteomyelitis of the ribs. Operation was proposed, but refused.

Four months later, she was again re-admitted with an abscess in the original situation. It was split open by an oblique incision, running from the ninth rib in the anterior axillary line, downward and inward to the left upper quadrant of the abdomen. At the abdominal extremity of the abscess cavity, a spicule of bone, about 2½ cm. long

and ½ cm. in diameter was found. It looked like a bit of chicken bone. The wound was packed and rapid healing followed. The pathological report reads: "The bone sliver has probably been present in the abscess cavity some length of time, as all the collogen substance has been digested, and only mineral substance remain."

TYPE VI.—*Inflammation and Obstruction in a Hernial Sac.*—Large irreducible hernias of all types are favorite sites for foreign body perforation. The kinks, angulations, and adhesions of the gut all favor the arrest of a foreign body. Judging from the statistics of Wölfler and Lieblein, these occurrences were much more common years ago, when early operation for hernia was less frequent, and large irreducible hernias more common than nowadays.

Both of the cases in our series occurred in large, irreducible umbilical hernias, one of which was a recurrent one. The clinical picture will vary, depending upon whether there is perforation with escape of the foreign body into the sac, or whether there is impaction in the lumen of the gut coincident with the perforation. In the former, the signs will be mainly those of local inflammation. See Case I. In the latter, there will be inflammation, plus signs of ileus. It is interesting to note that in both of the cases reported below, where the large ventral hernias were practically subcutaneous, the signs of phlegmon of the abdominal wall were so marked that there was considerable discussion before operation as to whether a hernia was actually present.

At operation, when the sac is opened, an abscess is usually encountered. When the signs of obstruction have been marked, simple drainage of the abscess is not sufficient. The loops of gut adjacent should be carefully palpated, and enterotomy performed if necessary to remove the foreign body. Close of the enterotomy may sometimes be impossible due to the friability of the intestine. In such cases, it may be advisable to use the opening for an enterotomy. Of course there should be no attempt at reduction or repair. Any manipulation, which might break down adhesions, separating the local process from the general peritoneal cavity, should be sedulously avoided.

CASE XII.—Mrs. A. H., age fifty-eight, was admitted to the Mt. Sinai Hospital, in May, 1923. She had had an umbilical hernia repaired four years ago. Her present illness began three days before admission with pain, redness and swelling around the centre of the abdomen. She had experienced chilly feelings, and her temperature had been elevated. There was no history of abdominal pain, vomiting or constipation. On admission, her temperature was 103° F. In the centre of the abdomen, there was a large, red, hot, tender, indurated area, about six inches in diameter, over which fluctuation could be detected. It was impossible to tell whether or not the hernia had recurred. A small vertical incision was made over the maximum point of fluctuation. A localized fecal abscess was encountered, and evacuated. The posterior wall of the abscess was formed by small intestines densely matted together. Two pieces of chicken bone, about one inch in length and one-quarter inch in diameter, were found lying free. The sites of perforation could not be discovered. Following drainage and subsidence of the acute inflammation of the abdominal wall, it was found that the patient had a large recurrent umbilical hernia. The wound healed rapidly, without any fecal discharge.

CASE XIII.—Mrs. H. W., age sixty-two, was admitted to Mt. Sinai Hospital, December 16, 1926. Her chief complaint was abdominal pain and vomiting, three days'

duration. She had always had a large pendulous abdomen. Four days before admission, she noticed that it was beginning to get hard in the centre, in contra-distinction to its usual flabby character. That night she experienced mild cramp-like, generalized abdominal pain. For the past two days she had vomited frequently. Examination revealed an obese, very acutely ill woman, with a rapid pulse, and in poor general condition, who was vomiting intestinal contents. The abdomen was large, pendulous, and greatly distended. The region around the umbilicus over an area of four inches in diameter was acutely inflamed and indurated. It could not be definitely determined whether a hernia was present. However, the case was thought to be a local strangulation within one of the lobules of the sac with peritonitis, or a perforating intestinal foreign body. A four-inch incision was made, extending above and below the umbilicus. Pus was encountered just beneath the skin. The incision was enlarged, and the pus was found to come from the sac of an umbilical hernia. There was no evidence of any strangulated intestine. Because of the marked obstructive symptoms, it was thought advisable to perform an enterostomy. In passing the tube, an obstruction was encountered about one and one-half inches from the opening of the intestine. This was investigated, and found to be a chicken bone. The bone was removed, enterostomy performed, and the abscess cavity drained. That night the patient suddenly died. Autopsy showed the cause of death to be due to coronary artery disease and nephritis. The loop of gut in her hernia, which had perforated, was terminal ileum. Apparently there had been two chicken bones, only one of which had been removed at operation. The other was *in situ* but not perforating. There was a dense coat of fibrin around the original perforation, which opened into an irregular sacculated cavity, containing fecal matter. The posterior wall of this cavity was formed by a mass of adherent small intestine. There was no evidence of involvement of the general peritoneal cavity.

SUMMARY

1. Perforation of small non-metallic foreign bodies, such as fish bones, chicken bones, or slivers of wood, occur most frequently in the large intestines, especially at the flexures and in the cæcum.

2. The condition is more frequent than is usually recognized. Of the twelve proven cases occurring at the Mount Sinai Hospital within the last ten years, nine were discovered in the last three years. The difficulties in recognition are due to the lack of any leading history, the failure to visualize this type of foreign body by the X-ray, and the wide variety in the clinical manifestations.

3. The condition may manifest itself in a variety of ways, of which the most common and important for the surgeon are:

1. Symptoms of acute peritonitis.
2. Localized intra-abdominal abscesses.
3. Intra-abdominal, usually peri-colonic, inflammatory tumors.
4. Tumor of the abdominal wall.
5. Abscess of the abdominal wall.
6. Inflammation and obstruction in a hernial sac.

4. In peri-colonic tumors, which do not invade the intestinal lumen, or cause stenosis, the possibility of the mass being a foreign body tumor should be considered. Recognition of this condition may decide the surgical indication, and avoid an unnecessary and hazardous surgical procedure, as removal of the foreign body and drainage, will suffice to effect a cure.

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A STUDY OF THE VARIATIONS IN THE TENSILE STRENGTH OF SILK SUTURE MATERIAL

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of Baltimore, Md.

A year ago great daily variation in the tensile strength of the silk thread used for suture material in the Johns Hopkins Hospital was suspected. A study was undertaken to determine the exact extent of these variations, their causes, and methods of eliminating them, if possible. This study yielded some rather interesting facts regarding the thread used, especially the effect of various methods of sterilization upon its tensile strength. The method of study and the observations made are here given in brief form, together with the recommendations for the preparation of silk thread for suture material which were suggested as a result of the study.

Method.—The method of study was simple and objective. Its purpose was to determine, first, the normal tensile strength of the silk thread supplied for suture material in the clinic, and, in the second place, to observe the variations in the tensile strength under various experimental conditions. The method of testing the strength of a given bit of thread was as follows: It was cut into a length approximately eighteen inches long. This was then looped over the smoothly rounded hook of a sensitive spring scale, the two ends approximated and grasped with a gloved hand, and steady traction made on the thread until it broke. The reading on the scale at the moment the silk broke, expressed in pounds, was designated as its "pulling strength". All the thread used was obtained from the same surgical supply house and was supposedly of the same grade and weight. Control tests of the thread and the scales were made before and after each group of experiments. A mechanical device on the scales permitted correction for the zero point before each test. There was no constant place at which the loop broke.

OBSERVATIONS

I. Thread taken from different spools varied greatly in tensile strength although the spools had identical markings.

Spool No. 1—Average "pulling strength"..... 7.0 lbs.
Spool No. 2—Average "pulling strength"..... 8.5 lbs.
Spool No. 3—Average "pulling strength"..... 9.0 lbs.
Spool No. 4—Average "pulling strength"..... 10.0 lbs.
Spool No. 5—Average "pulling strength"..... 10.5 lbs.

II. The thread on any given spool, however, was practically uniform throughout. Tests were made at intervals of ten yards over practically the entire length of a number of spools.

For example:

Spool No. 1—"Pulling strength"..... 7.0 lbs. on repeated testings
Spool No. 2—"Pulling strength"..... 8.5 lbs. on repeated testings
Spool No. 3—"Pulling strength"..... 9.0 lbs. on repeated testings
(And so with other spools.)

III. Immersing the silk thread in cold water for fifteen seconds caused an immediate loss in "pulling strength" of approximately 20 per cent.

For example:

Before wetting—"Pulling strength"..... 10.5 lbs.
"Pulling strength"..... 10.5 lbs.
"Pulling strength"..... 10.5 lbs.
"Pulling strength"..... 10.5 lbs.

Average ..... 10.5 lbs.

Immediately after wetting with cold water for 15 seconds—
"Pulling strength"..... 8.5 lbs.
"Pulling strength"..... 8.5 lbs.
"Pulling strength"..... 8.5 lbs.
"Pulling strength"..... 8.5 lbs.

Average ..... 8.5 lbs.

IV. Immersing the silk thread in boiling water reduced its pulling strength but slightly more than immersing it in cold water did.

For example:

(*a*) Before wetting—"Pulling strength"..... 10.5 lbs.
(b) After wetting in cold water—"Pulling strength"..... 8.5 lbs.
(*c*) After wetting with boiling water for 15 seconds—
"Pulling strength"..... 8.5 lbs.
"Pulling strength"..... 8.0 lbs.
"Pulling strength"..... 8.0 lbs.
"Pulling strength"..... 8.5 lbs.

Average ..... 8.25 lbs.

(*d*) After boiling in water for 1½ minutes—
"Pulling strength"..... 8.5 lbs.
"Pulling strength"..... 8.5 lbs.
"Pulling strength"..... 8.0 lbs.
"Pulling strength"..... 8.0 lbs.

Average ..... 8.25 lbs.

(*e*) After boiling for 5 minutes—
"Pulling strength"..... 8.0 lbs.
"Pulling strength"..... 8.0 lbs.
"Pulling strength"..... 8.0 lbs.
"Pulling strength"..... 8.5 lbs.

Average ..... 8.12 lbs.

V. Silk thread which had been wet regained its original "pulling strength" if dried.

For example:

Before wetting—"Pulling strength"..... 10.5 lbs.
"Pulling strength"..... 10.5 lbs.
"Pulling strength"..... 10.5 lbs.
"Pulling strength"..... 10.5 lbs.

Average ..... 10.5 lbs.

After wetting —" Pulling strength"	8.5	lbs.
" Pulling strength"	8.5	lbs.
" Pulling strength"	8.5	lbs.
" Pulling strength"	8.5	lbs.
Average	8.5	lbs.
After drying— " Pulling strength"	8.5	lbs.
" Pulling strength"	10.5	lbs.
" Pulling strength"	10.0	lbs.
" Pulling strength"	10.5	lbs.
Average	10.4	lbs.

VI. Sterilization in a steam autoclave did not cause a loss in the " pulling strength " of the silk thread, provided that all of the live steam was withdrawn from the sterilizer before the thread was removed. If this precaution was observed there developed no consolidation of moisture on the thread after its removal from the warm sterilizer.

For example:

Before sterilization—" Pulling strength"	10.5	lbs.
" Pulling strength"	10.5	lbs.
" Pulling strength"	10.5	lbs.
" Pulling strength"	10.5	lbs.
Average	10.5	lbs.
After sterilization—" Pulling strength"	10.5	lbs.
" Pulling strength"	10.5	lbs.
" Pulling strength"	10.5	lbs.
" Pulling strength"	10.5	lbs.
Average	10.5	lbs.

VII. Immersing the silk thread in mineral oil did not cause a loss in " pulling strength."

For example:

Before moistening—" Pulling strength"	10.50	lbs.
" Pulling strength"	10.50	lbs.
" Pulling strength"	10.50	lbs.
" Pulling strength"	10.50	lbs.
Average	10.50	lbs.
After moistening—" Pulling strength"	10.50	lbs.
" Pulling strength"	11.00	lbs.
" Pulling strength"	11.00	lbs.
" Pulling strength"	10.50	lbs.
Average	10.75	lbs.

It is interesting that the oiled silk is apparently stronger even than the dry silk.

VIII. Heating silk thread in oil, even for a prolonged period of time, did not cause a loss in " pulling strength." (The oil in these experiments was heated to 110° C., that is, just below the boiling point for the oil.)

For example:

Before wetting with oil—"Pulling strength"—Average, 10.5 lbs.

After wetting with oil at room temperature—"Pulling strength"—Average, 10.50 lbs.

After wetting with oil at 110 degrees (C) for 1½ minutes—

"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.

Average ..... 10.5 lbs.

After heating in oil at 110° C. for 5 minutes—

"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 11.0 lbs.
"Pulling strength" ..... 11.0 lbs.

Average ..... 10.75 lbs.

Here again it was noted that the silk was apparently stronger after being oiled than before.

IX. Oiled silk thread did not lose its "pulling strength" when immersed in water.

For example:

Before oiling— "Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.

Average ..... 10.5 lbs.

After oiling and immersing in water—

"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.
"Pulling strength" ..... 10.5 lbs.

Average ..... 10.5 lbs.

X. Waxing silk thread did not protect it quite so well from the effects of moisture as oiling did.

Before waxing—"Pulling strength" ..... 10.50 lbs.
"Pulling strength" ..... 10.50 lbs.
"Pulling strength" ..... 10.50 lbs.
"Pulling strength" ..... 10.50 lbs.

After waxing and immersing in water—

"Pulling strength" ..... 9.5 lbs.
"Pulling strength" ..... 9.5 lbs.
"Pulling strength" ..... 9.5 lbs.
"Pulling strength" ..... 9.5 lbs.

Average ..... 9.5 lbs.

PRACTICAL CONSIDERATIONS

As a result of these studies, the following suggestions were offered for the sterilization and preparation of silk thread for suture material:

(1) *First,* that only thread from tested spools be used.

(2) *Second,* that the thread thus selected should be "dry sterilized" (in a steam autoclave) rather than by the older method of boiling in water.

(3) *Third,* that the thread should be moistened with sterile mineral oil after it had reached the operating table, and before it was exposed to the moisture of the tissues of the operative field.

It was estimated that adherence to these suggestions would eliminate, to a great degree, daily variations in the tensile strength of the suture material, and would increase the average effective strength of the sutures placed from 50 to 100 per cent. For the past year these suggestions have been adopted as routine for the preparation of silk suture material on one of the major divisions of the surgical clinic. The results have been satisfactory, and have justified the procedures.

SUMMARY

1. Some facts regarding the variations in tensile strength of silk thread under various conditions have been reported.

2. The application of these facts to the preparation and sterilization of silk thread for suture material has been indicated.

BRIEF COMMUNICATIONS

CONGENITAL HERNIA OF UMBILICAL CORD

THE rarity of such a hernia, the clinical course and interesting anatomical findings, make the following case worthy of record.

In congenital umbilical hernia, the only structures making up the sac are the thin transparent Wharton's jelly and the parietal peritoneum. Failure of agglutination of the umbilical plates during fetal life, leaving a free opening in the peritoneal cavity leading into the umbilical cord, is responsible for the condition. It occurred in about one out of 5184 hernias, according to Lundfos. In the Ruptured and Crippled Hospital, in eighteen years they have had four cases in 75,000 hernias. In 92 laparotomies recorded up to date, 29 died, a mortality of 31 per cent.

Treatment.—If the hernia is of small size and easily reducible after replacing the contents, the cord may be ligated close to the skin junction and a pad applied over the umbilicus to be held in place by adhesive strips.

In large hernias, operation is advisable. Incise Wharton's jelly down to peritoneum, strip peritoneum away from Wharton's jelly down to ring and close peritoneum with fine catgut. Approximate the raw surface including all layers at the umbilical opening, with mattress sutures, and dress daily. In some cases, it may be necessary to incise the peritoneum in order to reduce the hernia and properly close it.

CASE REPORT.—Baby G., first child, normal pregnancy, normal delivery. The family physician, Dr. Frances Kardons, who delivered the case at the Borough Park Maternity Hospital (July 6, 1927) noticed as soon as the child was born, a hernia of the umbilical cord. Aware of the danger of injury to its contents, she clamped the cord about seven inches away from the umbilicus, and delivered the placenta.

The writer was then requested to see the case in consultation and he examined the child forty-five minutes following its birth. Findings: Male, normally developed, weighing 8 pounds, lusty cry. The umbilicus was about one inch in diameter. The umbilical cord was much wider, spreading out like a mushroom or an inflated finger cot. The sac was completely transparent and about the size of a tangerine orange. Through the Wharton's jelly and peritoneum, which constituted the sac, one could plainly see, as if through clear glass, the contents of the hernia. It consisted of three coils of small intestine, in all about eight inches long, and the appendix about four inches long, about the thickness of a goose quill. The blood-vessels of the mesentery of the intestine and appendix could be plainly seen pulsating. The intestine was constricted at the neck of the sac and appeared irreducible.

The baby was taken to the United Israel-Zion Hospital and was operated on about one and one-half hours following its birth. The skin and umbilical cord were considered practically sterile, therefore requiring very little further preparation. However, a weak solution of tincture of iodine was applied to the field of operation. An incision was made in the Wharton's jelly and peritoneum, extending for one-half inch upward into the upper portion of the skin and fascia of the umbilicus. The intestine together

with the appendix was then replaced into the peritoneal cavity. The umbilical cord was cut at its cutaneous junction. The umbilical vein and the two umbilical arteries were ligated. The abdominal opening was large enough to admit two fingers. It was closed by through-and-through mattress sutures of silkworm, interrupted, including all layers, the skin, fascia and peritoneum. The umbilical opening was closed in a transverse direction, thereby lessening the chances of separation. The appendix continually persisted in protruding from the abdomen until the last stitch was inserted. A continuous catgut suture was then used to approximate the peritoneum and the raw edges

FIG. 1.—Congenital hernia of umbilical cord. Before and after operation.

of skin and fascia at the umbilicus. Dressing was applied, covered with two strips of adhesive and umbilical band. The operation lasted about eight minutes. No anæsthetic was used. The baby remained in good condition, apparently minding the procedure very little. The same day, shortly after operation, the child was taken back to its mother at the Maternity Hospital for its feedings. During her entire stay at the hospital, the mother was unaware of anything abnormal relative to her child.

Post-operative Course.—Bowels moved daily. Very little vomiting, no more than occurs with the average newborn. Temperature normal. Wound dressed daily, healing by primary union. Silkworm sutures removed on eighth day. Wound healed completely. At two weeks, the umbilicus has normal appearance, the infant appears healthy and is gaining weight.

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THE MANAGEMENT OF WOLFE GRAFTS

The use of the Wolfe graft is now an accepted part of the armamatarium of the plastic surgeon. Chief among the difficulties of technic encountered in their use is the suturing of this slippery graft on a slippery bed. Irregular and indifferent suturing is a common fault.

There are three necessary requirements for a successful "take": firm apposition, restoration of normal tension and accurate coaptation of the edges. It is with the latter requisite that the average surgeon discovers a stumbling block. Once dissected free, the graft is with difficulty sutured to

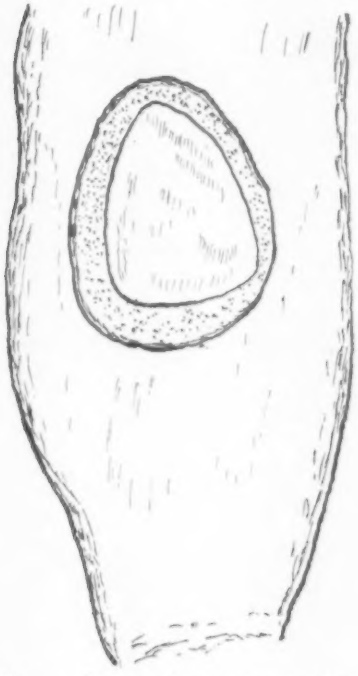

FIG. 1.—Graft cut from pattern to exact size of defect. Shrinkage may be noted.

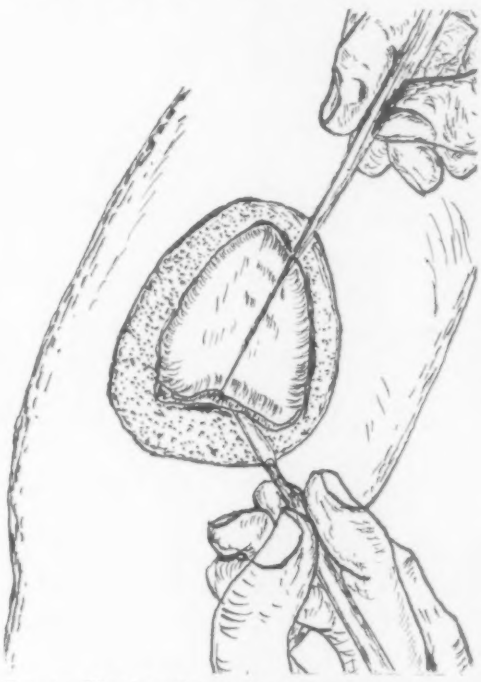

FIG. 2.—The edges of the graft are dissected free, leaving the base, or central portion still attached.

its new bed. Proper coaptation of the edges insures normal tension provided the graft is cut to the exact size of the defect and not one-sixth to one-half a size larger as most text-books advise.

During the cutting of these grafts, they curl and shrink to almost half the original size. The under surface becomes moist and slippery and the patience of even the most skilful surgeon is sorely tried before the graft is accurately sutured to the defect. This is especially true if the "non-touch" technic is employed. The following technic offers a solution to the difficulties encountered.

A pattern is cut to the exact size of the defect, using heavy tinfoil or thin sheet lead. The pattern is placed on the area selected and the graft outlined with the point of a knife. Small tissue hooks are now used to raise the edge of the graft and dissection along the edges is completed, leaving the

central portion still attached. Only a small amount of undercutting is used.

When the edges are freed, sutures are placed through them, using horse hair on a fine sharp cutting needle. The fine tissue hooks are useful in straightening the curled edges while the sutures are being placed. As many sutures may be used as desired. If the final suture is to be a continuous one, place from six to eight of these fixation sutures in the graft. If interrupted sutures are to be used, they may all be placed at this time.

The ends are left long and clamped together. If the needles are tied in they may be left, attached to the sutures, thus avoiding the necessity of

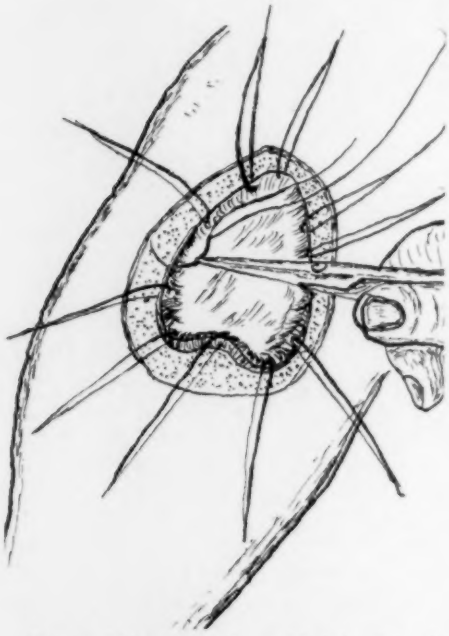

FIG. 3.—The sutures to be used in fixing the graft to its new bed are inserted through the edges. If needles are tied in, they may be left. The sutures are clamped together and used as a handle while completing the dissection.

FIG. 4.—The graft is quickly and easily sutured to its new bed at normal skin tension, without danger of displacement or loss.

re-threading. Using the sutures as a handle, the dissection is continued until the graft is freed from its base and carried to the area to be covered. Here it is properly adjusted and, using the needles already in place, the sutures are carried through the skin margins of the defect.

Advantages of this method are:

1. Minimal trauma to the graft.
2. A firm base through which the sutures may be placed.
3. Accurate placement of sutures, insuring better coaptation.
4. Permits employment of the "non-touch" technic.
5. Eliminates danger of dropping the graft.

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ACTINOMYCOSIS OF THE HARD PALATE

This case is reported on account of the unusual location of the disease. Arthur H. Sanford and Minna Voelker, who have collected and tabulated all reported cases in their article, "Actinomycosis in the United States," published in the *Archives of Surgery*, vol. xi, No. 6, have found no case in this situation. John Ruhrah in the ANNALS OF SURGERY, vol. xxx, p. 442, says: "The disease may occur as an ulceration of the mucous membrane lining the mouth. There have been two such cases in this country. In both the peculiar discharge led to a diagnosis. In one of the cases it extended through the cheek after having existed in rather a quiescent state." The detailed reports of both cases show that the lesions were situated on the mucous membrane of the cheek.

My patient, W. R. C., age forty-three, white, married, the proprietor of a country store, first came under observation December 1, 1926. His family history is negative except that one brother died with "miners' consumption". At sixteen years of age he had a gastric hemorrhage of unexplained origin. He has had no operation or other sickness. There is no history of venereal infection. For years he had made a practice of carrying a straw in his mouth.

About seven months previously he had injured the roof of his mouth with a splinter which he extracted himself. This bothered him for a few hours only. Four weeks before, a dentist who was extracting some of his teeth informed him he had some serious trouble with his palate. He had no subjective symptoms, however, and there was no history of cough or expectoration. There had been no recent loss of weight.

The patient was a spare active man whose physical examination was negative, except for the mouth, from which all the teeth had been recently extracted. The palate was high and sharply arched, and at the angle there was an elevated granulomatous, honeycombed swelling 1 x 2 cm. in size. Pressure caused the discharge of whitish-yellow pus from several points and slight bleeding. Neither probe nor X-ray showed any dead bone. The mouth was otherwise normal and there were no enlarged cervical glands. Dr. J. L. Lattimore reported the pus contained actinomyces and that the blood Wassermann was negative. Liberal doses of iodide of potassium and five radium treatments over a period of four months resulted in improvement but no cure. On May 2, 1927, under general anæsthetic an electric cautery was thoroughly applied to the affected area. This resulted in a prompt cure.

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EPITHELIOMA OF THE CERVIX ASSOCIATED WITH CARCINOMATOUS CYSTADENOMA OF THE OVARY*†

Major, in 1918, in an extensive review of multiple primary malignant tumors, studied 628 cases reported in the literature. He found that multiple primary malignant tumors do not have a predilection for organs of the same system, except paired organs, which is in marked contrast to their predilection for single organs. Major also observed that malignant new growths were more common in unrelated organs. The case of multiple malignant tumors

* Submitted for publication, September 28, 1927.

† From the Section on Surgical Pathology of the Mayo Clinic.

of the pelvic organs which we are reporting is of a type which he rarely found, that is, multiple malignant neoplasms in organs of the same system. Major's data revealed that the uterus was the most common site of two tumors of different types, next in frequency the breast and thyroid gland. The most common combination of malignant neoplasms was carcinoma and sarcoma.

Owen, in 1921, studied multiple malignant tumors reported in the previous ten years and found that in 3000 cases of carcinoma, approximately 4.7 per cent. were multiple. Basal-cell epithelioma was most frequently multiple, next in order basal cell and squamous-cell carcinoma, then multiple squamous-cell carcinoma, multiple carcinoma of the breast and then carcinoma of the breast with some other type of carcinoma. In these reports or in other cases in the literature,[3, 4, 5] we were unable to find a case similar to the one presented here.

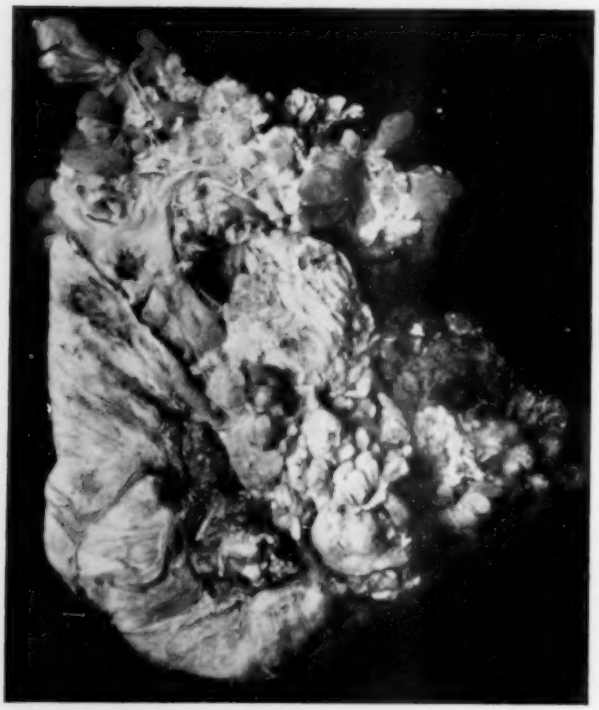

FIG. 1.—Carcinomatous papillary cystadenoma of the ovary.

CASE.—A woman, aged fifty-seven years, the mother of four living children, came to the Mayo Clinic because of a mass in the lower part of the abdomen, which had been noticed about three months previously. The family and personal history were unimportant. The climacteric had been passed nine years previously. About five months before examination she noticed urinary frequency, urgency and nocturia accompanied by suprapubic pain which was severe during micturition. These symptoms persisted for two or three weeks and then disappeared. A mass was noticed about six weeks later. An occasional foul purulent vaginal discharge without bleeding followed the first symptoms. Later about 5 c.c. of stringy blood came from the vagina on one occasion after voiding. At the time of admission there were no urinary complaints. The appetite was good and the bowels were regular. There was no appreciable loss of weight.

Physical examination was negative except for a slightly tender, rounded abdominal tumor which extended nearly to the umbilicus. On vaginal examination the entire pelvis was filled with a lobulated but not definitely tender mass. The fundus could not be made out. There was some bleeding following examination. Exploration of the abdomen was advised.

At operation the uterus was found to be enlarged to about the size of a six months' pregnancy and felt cystic. There was considerable inflammatory reaction in the pelvis.

When the cervix was cut across mucoid material escaped from the uterus. After malignancy was determined the cervix was completely removed. There was a cyst in the left ovary about 14 cm. in diameter which contained mucopurulent material. The pelvis was carefully washed with large quantities of water and drainage instituted. On the second day after operation pulmonary complications developed which resulted in death five days later.

At necropsy bronchopneumonia and pulmonary œdema, and fatty changes in the

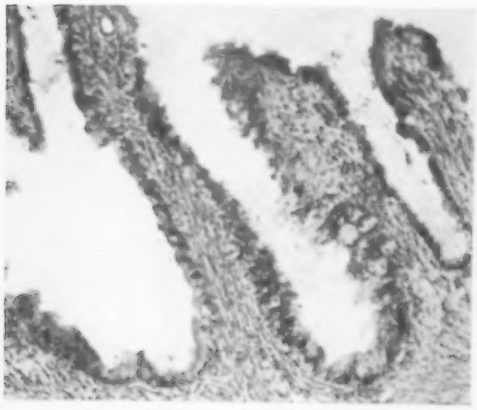

FIG. 2.—Carcinomatous cystadenoma of the ovary. (x 60.)

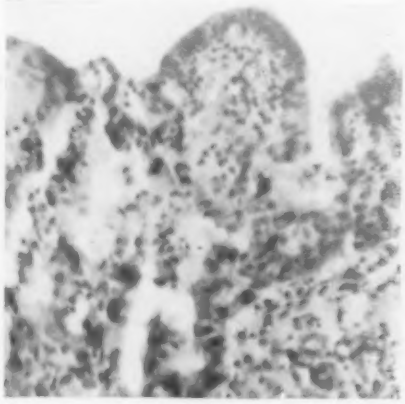

FIG. 3.—Metastasis of the ovarian tumor to the uterus with polymorphonuclear leucocytes in the spaces of the tumor. (x 120.)

liver associated with chronic diffuse nephritis, were noted. Careful search failed to reveal evidence of metastasis from the carcinomas removed at operation.

The specimen removed at operation weighed 580 gm. The left ovary contained

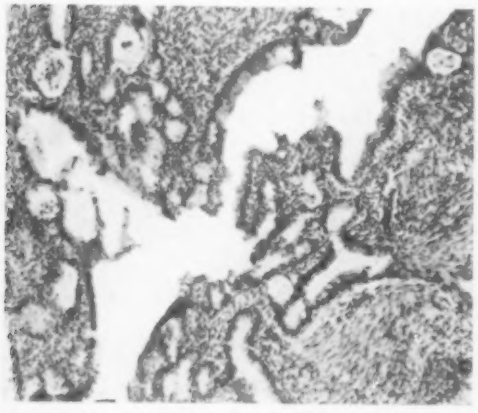

FIG. 4.—Metastasis of the carcinomatous cystadenoma of the ovary to the cervix. (x 60.)

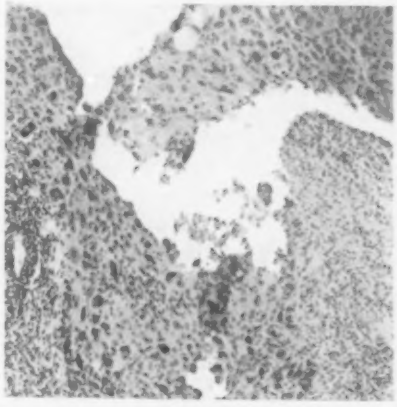

FIG. 5.—Squamous-cell epithelioma of the cervix graded 4. (x 60.)

a malignant papillary cystadenoma, approximately 8 by 8 by 12 cm., which involved the whole inside of the ovary (Fig. 1). The right ovary was small and atrophic. The uterus contained a quantity of purulent material and mucus.

The tumor of the ovary was composed of fibrous connective-tissue stroma covered by a layer of epithelium of varying thickness (Fig. 2). The cells of this epithelial covering were large with one or more nucleoli, characteristic of malignant cells. The stroma of some of the papillæ was myxomatous. In the spaces of this ovarian tumor

were polymorphonuclear leucocytes. On the surface of some of the sections was a mucoid-like substance.

The lining of the uterus was composed of a varying number of layers of epithelial cells with the large nucleus and nucleolus of malignant cells.[5] In general they were much like the cells described in the ovarian tumor. Interspersed among these malignant cells were a great many polymorphonuclear leucocytes, which supported the gross diagnosis of pyometrium (Fig. 3).

In the cervix similar malignant cells were present (Fig. 4). There were also areas of large hyperchromatic squamous cells invading the substance of the cervix. A few of these cells contained a little keratin, but most of them were undifferentiated. This squamous-cell epithelioma was graded 4, according to Broder's classification (Fig. 5).

COMMENT.—When two related tumors are found in the same organ, the question always arises: Is this an example of metaplasia, or are there two distinct primary tumors? In this case we feel reasonably certain that the two neoplasms were not the result of metaplastic activity of the cells of the carcinomatous cystadenoma, for the epithelioma in these sections could be traced directly from the basal layer of the cervical epithelium. In no place in the sections were the two tumors changing from one type to another.

Similar multiple malignant tumors in the same organ may be caused by carcinoma arising from several centres simultaneously, and later these may coalesce. Multiple tumors of the same kind may be a concidence or the result of metaplasia.

Careful routine examination of operative specimens in many instances will reveal multiple malignant processes.

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THE TECHNIC OF RECTAL ANÆSTHESIA IN GOITRE SURGERY*

For the past two and one-half years, Gwathmey's rectal anæsthesia has been used in preference to other types of anæsthesia in practically all the goitre cases operated on by me at the New York Post-Graduate

* From the Goitre Clinic of Dr. Charles Gordon Heyd at the New York Post-Graduate Medical School and Hospital.

Hospital. This series is rather small, numbering thirty-four at the present time, but the results have been so uniformly satisfactory that rectal anæsthesia would seem to have a very important place in thyroid surgery.

Technic.—Time of operation: two P.M.

Pre-operative Treatment.—At eight P.M. the night before operation, the patient receives pulv. glycerrhizæ drams two to three. At seven A.M. the morning of operation, a soap suds enema is given. This is followed immediately by a colonic irrigation of warm water. This irrigation is to be administered until the return is absolutely clear, from six to ten gallons of water being used. This should be completed not later than nine A.M. At nine-fifteen A.M., morphine sulphate grains one-eighth, one-sixth, or one-fourth is given, the amount of the dose depending on the body-weight of the patient. The patient is to remain in bed from that hour on. At twelve noon, chloretone grains fifteen, ether drams two, and olive oil drams four is administered through a rectal tube which has been inserted eight to ten inches above the anus. The tube is clamped but allowed to remain in the recto-colon. The patient is placed in a left Sims' position and allowed to sleep. At twelve-fifty P.M., a second dose of morphine grains one-eighth, one-sixth, or one-fourth is given, plus atropin grains one-one hundred and fiftieth. This dosage is governed by the patient's reaction to the previous medications. The nurse is in charge of all treatment up to this point.

Administration of Anæsthesia.—At one P.M. a mixture of olive oil ounces two, ether ounces six, and paraldehyde drams one, is introduced through the rectal tube which has remained in from the previous medication. The patient should receive one ounce of this mixture per twenty pounds of body-weight, at the rate of one ounce every five minutes, or a total of forty minutes for the introduction of an eight ounce mixture. The tube should be on a level with the patient for the expulsion of gas. If the patient complains of cramps, or the desire to evacuate bowels, it will be necessary to stop the flow of the solution and lower the tube for the escape of flatus. When the required amount of mixture has been given, the tube is clamped and allowed to remain in the rectum throughout the operation. If the patient has not been narcotized by the time the mixture has been introduced into the rectum, the anæsthetist may allow her to re-breathe through a Bennett inhaler. This prevents the loss of the anæsthetic through the expired air. One must be careful that the mask does not touch the patient's face while conscious. If it ever becomes necessary, a small amount of ether may be added to the Bennett inhaler until the operation is started. We have never had to keep the patient anæsthetized longer than forty minutes by this method, but Miss Smith has kept one patient under in this way for one hour and forty-five minutes. As soon as the operation has been completed, the tube which has remained in the rectum is unclamped and any remaining mixture is drained off.

Post-operative Treatment.—The patient is returned to her room and a cold colonic irrigation of from four to six gallons is given at once. This is

followed by a retention enema of olive oil, two, four, or six ounces. It is best not to use a Murphy drip with a patient who has had rectal anæsthesia. A hypodermoclysis of one thousand c.c. of saline is administered immediately after completing the colonic irrigation, which is absorbed before regaining consciousness. The patient may receive morphine grains one-eighth, one-sixth, or one-fourth, when necessary. In cases of hyperthyroidism of the Graves' type, Lugol's solution drams one-half is given, as soon as the patient can swallow. If the patient is critically ill, Lugol's solution drams two or three may be used in a retention enema on completion of the colonic irrigation.

This series of cases includes five substernal goitres, seven adenomas without hyperthyroidism, and five adenomas with hyperthyroidism. The highest metabolic rate was plus fifty-four and the lowest plus eleven, the average being plus thirty-one and one-half. There were seventeen cases of exophthalmic goitre or Graves' disease, of which the highest metabolic rate was plus ninety-six and the lowest plus twelve, with an average of plus forty-eight and one-tenth. In this series of cases, there have been no complications such as pneumonia, bronchitis, or gastro-intestinal disturbance, resulting from the rectal anæsthesia.

Conclusions.—1. The cases of exophthalmic goitre make an exceedingly smooth post-operative recovery. 2. The substernal goitres are delivered with much less bleeding than by either nitrous oxide, or ethylene anæsthesia.

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BOOK REVIEWS

Surgical Diseases of the Gall-bladder, Liver, and Pancreas, and Their Treatment. By Moses Behrend, M.D., 8vo, cloth, pp. 250. Philadelphia, F. A. Davis & Co., 1927.

The author presents as a monograph an elaboration of numerous contributions on gall-bladder surgery which have appeared in current medical journals.

Perusal of this volume conveys to one familiar with surgical literature that it mirrors the teachings of Deaver; furthermore, it is preëminently clinical in its exposition; to witness the exclusion of laboratory methods as aids to diagnosis. We welcome finding its pages unencumbered with the history of past performances, since the personally tried and tested everywhere prevails, and it is only by the mention of a name appearing in the text and accounted for in an adequately appended bibliography, that a connecting link with the historical past is established.

The chapters on Anatomy, Pathology, and Physiology are collaborated by authorities in their respective fields in the first five chapters embracing nearly half of the book, thus constituting an essential foundation for the didactic presentation of the subject matter, complementary to which are abundant illustrations.

Chapter III on the Anatomy of the Ducts and Blood-vessels must be regarded as an outstanding feature of this book. The story thereof is succinctly told in five pages, the remaining forty-five by virtue of the excellent full page drawings very graphically reveal the anomalies. It is worthy of note that such appeared in advance of the surgical narrative. As a rule the anomalous is treated anomalously and mentioned *en passant* or at the end; but here it occupies a foremost place and rightly so when one reads that there are 25 per cent. of duct variations and 50 per cent. of vascular departures from the normal.

The author logically aligns his attack on the gall-bladder by what he designates the "open method" as opposed to the "blind method". This implies singling out the biliary and vascular pedicle through an incision in the right free border of the gastro-hepatic omentum. To quote "this is the logical method when comparison is made with other organs requiring removal."

Infection as the ultimate cause of gall-bladder disease is so nearly universally conceded that it is not material for issue, but whatsoever we know of the infectious origin of stones should have been supported by a brief reference to the classical work of Bacmeister and Aschoff. Our under-

standing of the mechanism of infection is not furthered by subdivision into primary comprising the organs, duodenum, appendix inclusive of the blood and secondary emanating from systemic diseases dispersing infection through the blood, in as much as the primary grouping may also be of hæmatogenous origin. That the bacterial examination of the bile as cultured at operation is usually sterile, exceptionally infectious, meets with apparent contradiction, that aspiration of the gall-bladder be not resorted to in collapsing the same lest escaping contents contaminate and fatal issue result.

Partiality toward nitrous oxid and oxygen in spite of admitted inadequate relaxation, to be overcome by manual dexterity, is buttressed by the needs for the same because of the frequent incidence of high blood-urea-nitrogen, and the increased liability of pneumonia where ether is used. Be that as it may, it should not have precluded the mention of novocain anæsthesia, regional, spinal or para-vertebral in the extremely sick gall-bladder patient for the performance of external drainage or internal drainage to be superceded by nitrous oxid and oxygen where more protracted work is called for.

That the gall-bladder may be the nidus of focal infection responsible for co-existing myocarditis is aptly stressed but conversely this fact should have been embodied in the chapter on differential diagnosis that epigastric distress concomitant of myocarditis should direct attention to the gall-bladder as the *fons et origo,* calling for surgical relief.

Radiography and cholecystography receive their proper evaluation in being limited to cases which not being clear-cut do not reveal themselves. The Lyons drainage is but faintly praised for its diagnostic value and not much more from a therapeutic standpoint. The Charcot syndrome is referred to as a diagnostic aid without precising the symptoms that characterize it. In this connection the omission of the law of Courvoisier for differentiating between carcinoma and stone should be noted since it has found a place in all dialectics on this subject.

In chronic jaundice with cholemia due to common duct obstruction other than stone, after adequate preliminary preparation, hepatico-duodenostomy is offered as the operation of choice save for the complicating pancreatitis where cholecystostomy is regarded as the operation specially indicated. Otherwise the author would relegate cholecystostomy to oblivion for he is an out-and-out exponent of ectomy. In few words, in no way departing from the usual limited interference for its relief, acute hemorrhagic pancreatitis is dismissed. Likewise cysts of the pancreas.

The final chapter is a thesis in experimental surgery "On Ligation of the Hepatic Artery," the outcome of which is dangerous at all times, thus substantiating its futility when applied to the human in few instances for aneurism or wound of the artery, because of the large areas of liver necrosis that ensue.

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1. Science and Practice of Surgery, by W. H. C. Romanis, F.R.C.S., Teacher of Practical Surgery, St. Thomas' Hospital, and Philip H. Mitchiner, F.R.C.S., Teacher of Operative Surgery, St. Thomas' Hospital. Large octavo; cloth; 2 vols.; pp. 795 and 955; New York, Wm. Wood and Co., 1927.

2. Surgery, Its Principles and Practice for Students and Practitioners, by Astley Paston Cooper Ashhurst, M.D., Professor of Clinical Surgery, University of Pennsylvania, 3rd edition, revised; large octavo; cloth; pp. 1179; Lea and Febiger, Philadelphia, 1927.

3. Manual of Surgery for Students and Practitioners, by Albert Carless, F.R.C.S., Consulting Surgeon, King's College Hospital, and Cecil P. G. Wakeley, F.R.C.S., Assistant Surgeon, King's College Hospital. Twelfth edition; large octavo; cloth; pp. 1544; New York, Wm. Wood and Co., 1927.

Of the surgical text-books appearing in the Fall of 1927, the book of *Romanis and Mitchiner* is an entirely new candidate for surgical approval. A notable feature of the London hospitals and medical schools is the appearance, from time to time, of text-books and manuals which, in a special degree, represent the standards of individual hospitals. So here we have the St. Thomas Hospital surgery; its authors, two of the younger members of the surgical staff and the book itself dedicated to the consulting surgeon at the same hospital, Sir George Makins, whom the authors characterize with affection as their friend and teacher.

A point which strikes the reader who consults this book is the fact that it is in two volumes, neither one of which is too large for comfort in handling. This is really a great convenience to appreciate which one has simply to consult one of the larger one-volume text-books of fifteen hundred and more pages and compare it with these volumes under review. We note with interest the reference by the authors to the multitude of chemical tests and laboratory examinations which are now employed in connection with surgical cases. They deplore that such methods should be used to establish a diagnosis so often with complete neglect and disregard of clinical aspects and personal subjective symptoms of patients. To this observation the reviewer wishes to add his full sympathetic assent. Not that he would have the laboratory work slighted at all, but that it should be used more than it is to confirm or correct the careful clinical diagnosis. One sees a special object in this book as a text-book for students in preparing for the various surgical examinations to which they may aspire in England in the arrangement that to many of the chapters a preface is furnished giving an account of the applied surgical anatomy or physiology of the organ discussed. It goes without saying that the book being a presentation of the surgery of one of the great London hospitals, is of interest and value.

One little point has attracted the attention of the reviewer which has gained undue importance possibly in the editorial mind in his own work in

A Treatise on Orthopedic Surgery, by Royal Whitman, M.D., M.R.C.S. Eighth edition, thoroughly revised. Large octavo; cloth; pages 1061. Philadelphia, Lea and Febiger, 1927.

The first edition of Whitman's treatise appeared in 1901. That the work has proved to be valuable and acceptable to Orthopedic surgeons and to all interested in the maintenance of bodily symmetry is shown by the frequent editions which have steadily appeared since that time. When Robert Osgood was reviewing the sixth edition in January, 1921, he declared the book to be the best American text-book on the subject. This opinion was based upon the clear and readable style of the author, the simple but yet sufficiently detailed pathological descriptions which it presented and the helpful elements of differential diagnosis which it contained, all leading up to descriptions of methods of treatment the excellent end results of which are the best criteria of their value. The first edition of the book was dedicated to Virgil P. Gibney, his chief in the work of the New York Hospital for Ruptured and Crippled, with the work of which institution Doctor Whitman was associated. With the advance of years, Doctor Gibney has withdrawn from active work and Doctor Whitman himself is the Surgeon-in-Chief of the hospital in which they labored together for many years. The increasing experience from such opportunities are embodied in this last and revised edition of the book. The author, in his preface, declares that a comparison of the present edition with the first demonstrates the great advance both in scope and method of orthopedic surgery during the last twenty-five years. The reviewer agrees in the claim that the book has gained in interest and authority with each succeeding issue.

Lewis S. Pilcher.

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